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Practical Pharmacy Edition

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COVER: Young men from Mexico, Central and South America are being trained in American pharmaceutical industry as part of the good neighbor policy. Candidates have been chosen for a number of industries through international boards sponsored by the office of the Coördinator of Inter-American Affairs. The photograph shows Pedro A. Reyes, who owns his own pharmacy in El Salvador, working in the Merrell Laboratories.

Editorial

NEW PUBLIC HEALTH BILL

LONG-needed legislative reform, a bill to codify the laws relating to the U. S. Public Health Service, has been placed before Congress by Rep. Alfred L. Bulwinkle of North Carolina. Since 1879, when it was established as a small corps of physicians to provide medical care for American merchant seamen, the Public Health Service has grown to be the central health organization of the government. And like the proverbial Topsy it just grew, picking up functions along the way through a host of statutory clauses. This whole hodgepodge, under which Surgeon General Parran has had to operate, would be repealed by the proposed bill (H.R. 3379). In its place would be one unified law correlating and clarifying all former functions.

Officials of the ASSOCIATION are taking steps to see that pharmacy as a public health agency will not be lost in the shuffle. The role of pharmacists in the Service, like all personnel, will be neither limited nor delineated. The personnel thus retains flexibility, which is controlled by appropriations granted for operation. It is hoped that under the new setup additional pharmacists would be commissioned and others given civil service status to take their places beside those already in the Public Health Service.

Although small in number, these men shoulder an important responsibility: to demonstrate the unique service which trained and capable pharmacists can supply as health officers. Thus the ASSOCIATION seemingly takes a disproportionate interest in such minority groups, for on their record will depend, to some degree, whether pharmacy will obtain neglected opportunities to demonstrate the varied services which the renascent profession is prepared to supply.

The proposed bill furthermore removes the limitation on rank applying to those in pharmaceutical service, which now corresponds to captaincy in the Army. At the same time the rating of the entering commission would be lowered from first lieutenant to second lieutenant, thereby opening the door to younger pharmacists with the four-year degree who are not now eligible.

Preliminary discussions, held recently with the Surgeon General, have not been primarily concerned, however, with pharmacists in the Public Health Service proper. They have emphasized the relationship between the government health program and the nation's pharmacists, and how to improve that relationship.

To what extent has the corner pharmacy coöperated in the local, state and national public health program? The answer of most of us will be, a feeble one. It helps little to point the finger of blame elsewhere. Rather it is time to make the corner pharmacy a real, as well as a titular, community health center. Projects such as the campaign against venereal disease show what can be done. Here we are seeking opportunities for more service rather than more profits, for in the long run both goals lead to the same end—except that the one takes the professional route.

The U. S. Public Health Service cooperates closely with the health departments of the states, and to some extent coördinates their health programs. State and local

pharmaceutical organizations can thus tie in with the national program by becoming better acquainted with their public health officials, seeking service on health boards and committees, and inviting speakers to pharmaceutical meetings to develop coöperative projects. Progress has been made but much remains to be done.

EXTENDING EDITORIAL SERVICE

THE blue pencil is handed to a new editor as the Practical Pharmacy Edition nears the fourth anniversary since it and its technical counterpart were born from the old journal of the ASSOCIATION. It will continue to be the professional publication of the retail and hospital pharmacist—practical in both the pharmaceutical and dictionary sense. Based on ASSOCIATION ideals, lifted with the rising tide of pharmacy, the JOURNAL can be expected to become an increasingly important aid to professional practice. Toward this end the editorial door is opened to criticism and comment, papers and suggestions dealing with every nuance of pharmacy.

Some claim there is no time to contribute to the literature as in more leisurely peacetime days, especially with curtailed section meetings. But publication of time-saving techniques, solutions to wartime problems of practice, and promising research reports will justify the time spent in preparation a thousandfold. Sharing our ideas and achievements will save the time of all, will save duplication of work and research, and improve health services during this period when they are most needed.

Besides bringing the latest in professional pharmacy to the pharmacist, the editorial offices now plan to assume a new function in also putting these and similar developments before the public to show the part the pharmacist is playing in the life of the nation in war and peace. At the Columbus meeting the ASSOCIATION resolved "that steps be taken to provide, through an adequate news service, for the dissemination of the information about the achievements of pharmacy to the other sciences and professions and to the public."

Tentative plans are being made, and a report will be submitted to the Council within a fortnight for approval. At the start, it is expected that news reports and photographs will be issued from the AMERICAN INSTITUTE OF PHARMACY to major news agencies and editors. Background information and interpretive comment will be supplied interested writers who sometimes hesitate to cover a good pharmacy story because they lack facts, or are not sure of the significance of the facts to the public. As the public relations program proceeds, it should be expanded in scope of coverage, in media used, and extent of distribution.

The editorial grist will thus be viewed from two angles; first, to evaluate its significance to pharmacy; second, to decide how it can help lift the bushel from the light of pharmacy. Although it is hoped that editorial results will justify approval, we point out that constructive criticism makes an editor bang the typewriter a little harder and often brings a journal just a little nearer the elusive goal of perfection.

THE WHITE HOUSE
WASHINGTON

October 25, 1943.

My dear Doctor Griffith:

It has come to my attention that National Pharmacy Week has been set for the week of November 1 - 7. Will you be good enough to extend for me my most sincere thanks to the American Pharmaceutical Association for the splendid work they have done in the war effort.

The high spot of this has been the collection of small quinine stocks throughout our Nation. I am advised that this amount exceeds four tons. In view of the marked shortage of this critical drug, you have done a very great act in bringing about the collection of this drug and turning it over to the Armed Services.

We are looking forward to your continued support of the Medical Departments of the Army and the Navy in the great work that is being done in saving human life.

Very sincerely yours,

Franklin D. Roosevelt

Dr. Ivor Griffith,
President,
American Pharmaceutical Association,
2215 Constitution Avenue, N. W.,
Washington, D. C.

A. PH. A. PRESIDENT'S

NATIONAL PHARMACY WEEK MESSAGE

by IVOR GRIFFITH

PRESIDENT, AMERICAN PHARMACEUTICAL ASSOCIATION

PUBLIC SHOWN THAT LIFE AND DEATH RESPONSIBILITY IS HIDDEN UNDER MERCHANDISING CANOPY

IVOR GRIFFITH

PHARMACY Week was originated by a clear-thinking, young practitioner of professional pharmacy, namely, the late Dr. Robert J. Ruth, and its first and foremost purpose was, and is, to inform the public in a dignified fashion that the pharmacist is more than a mere merchant.

For many, many years the scientist around the corner has been, for reasons not of his own choice, hiding his light under a bushel. The purpose of Pharmacy Week is to *remove that bushel!*

There was a time when the corner druggist made all his own medicines, powders, pastes unguents and pills. Now the pharmaceutical factory makes them—tons at a time, and carefully, accurately and cleanly, with the latest and best scientific production methods and control facilities.

Once upon a time, the corner pharmacist prepared not only the prescription, but also every ingredient in the prescription. But now, more than often, he takes standardized ingredients made elsewhere, and combines them with skill, into the prescription which enters the sickroom, and mind you, he is equally responsible with the doctor for the safety of that prescription.

However, since this natural tendency in the practice of pharmacy turned much of the practitioner's duties into other hands, namely, into large-scale manufacture, the corner druggist had to search for other outlets for his energy and for his service, to say nothing of the return upon his investment in education and in equipment. And so, he had to build around his professional work a supporting merchandising program. He had to do this in order to be able to continue serving the public as the safe and legal handler of medicines.

Pharmacy Week is dedicated to showing the public that there is a life and death responsibility hidden beneath the canopy of merchandising which seems to hide the real service of the corner drug store.

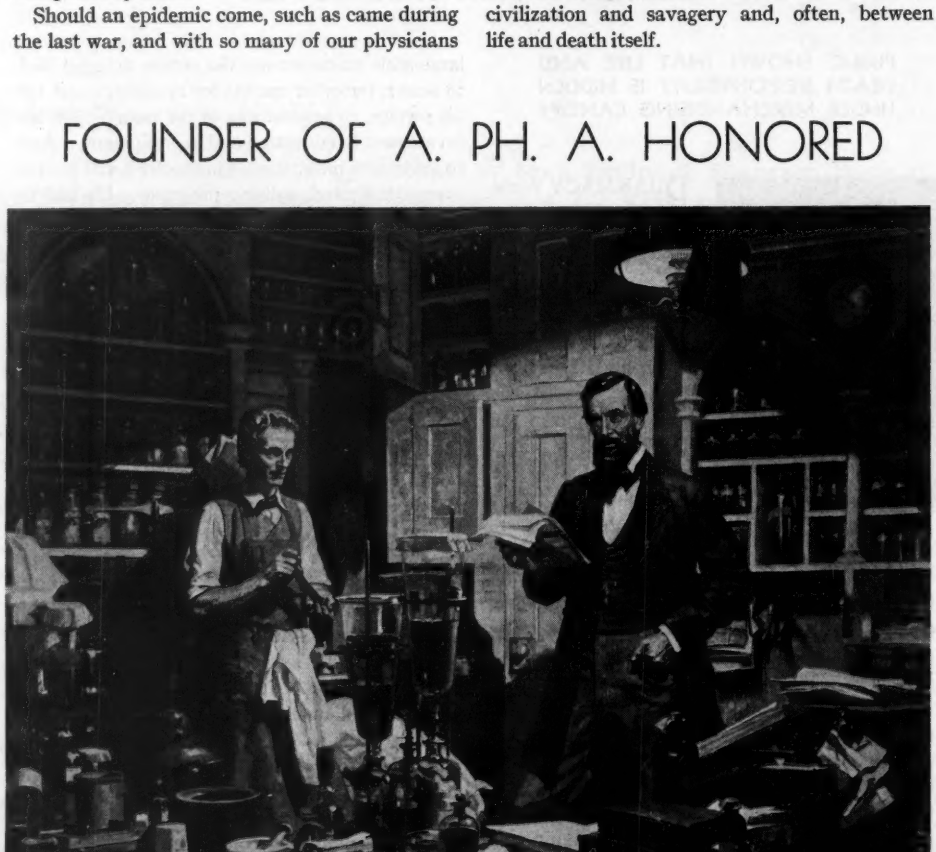
Of course, we do see establishments that have tinselled their performance in such a way that they no longer look like drug stores, but more like notion shops. But the real pharmacy of today is not represented by blatant, price-cutting, cheap, notion and novelty shops, masquerading as pharmacies, but rather by those dignified and honest neighborhood drug stores whose reputation has been established through loyal, helpful service in every stable American community.

I was recently asked, and rather sarcastically, to explain what I meant when I referred to pharmacy's contribution to the war "action." In response I called attention to the aftermath of the Salerno beach-head battle, and the sharply lessened number of casualties resulting because the injured recovered so quickly. My answer was countered by his compliment to the doctors, surgeons and nurses who were on the job, with which I, of course, agreed. But what he had failed to recognize was that it was the blood plasma, the sulfonamides, the antiseptics, etc., which had revolutionized the treatment of the injured and produced the results at that amphibious engagement, where only one per cent of the injured failed to recover. And, furthermore, my querist had also failed to recognize that it was the research and production departments of the large pharmaceutical houses that had developed and supplied these vital drugs, supplied them

in prodigious quantities, and with every unit made dependable through assiduous control. America would have a new conception of pharmacy if every citizen might have a chance to visit the research and manufacturing departments of the great American drug houses, to see the workers in action, to see the purpose of these fine establishments, and know the good that is being accomplished.

Should an epidemic come, such as came during the last war, and with so many of our physicians and pharmacists called to the service, I am certain that those who are left behind would give as valiant and significant a service to their neighbors as was rendered during the terrible epidemic previously mentioned. And it is my hope that Pharmacy Week will arouse a greater public appreciation of the contribution of this profession day in and day out as it provides the community with the things that make the difference between civilization and savagery and, often, between life and death itself.

FOUNDER OF A. PH. A. HONORED



WILLIAM PROCTER, Jr., founder of the AMERICAN PHARMACEUTICAL ASSOCIATION and famed for his drug standardization work, was paid tribute by the 250 distinguished pharmacists, medical men and scientists gathered in Philadelphia on Nov. 5 for the unveiling of a painting depicting Procter at work in his laboratory. The painting, which is reproduced above, is the fifth in a series by Dean Cromwell on "Pioneers of American Medicine."

Dr. Ivor Griffith, president of the AMERICAN PHARMACEUTICAL ASSOCIATION, was the principal speaker at the ceremonies. Ensign Melba Grafius of the WAVES, fifth youngest woman pharmacist in Pennsylvania, unveiled the canvas, entitled "Father of American Pharmacy."

Perhaps Procter's chief contribution to pharmacy was the standardization of drugs, long needed because of the varying efficacy of compounds due to different methods of preparation. His researches led to the publication of more than 500 technical papers. He was also editor of the *American Journal of Pharmacy* for 20 years, making it what is considered the most complete history of the progress of pharmaceutical science in the United States during that period.

As founder of the 90-year-old AMERICAN PHARMACEUTICAL ASSOCIATION, Procter established an organization that was to be the leading proponent of the scientific accuracy and high standards of professional integrity for which he stood. Procter's name occupies a prominent place in all the proceedings of the ASSOCIATION from the first meeting in Philadelphia, October, 1852, to the Richmond convention of 1873. The only annual meeting he missed was in 1866 when he went to Paris as a delegate to the International Pharmaceutical Congress. Death came to the father of American pharmacy in 1874 at the age of 56.

The painting which honors his works is the result of a plan conceived by Frank F. Law, president of John Wyeth and Brother, while a Navy medical corps pharmacist during the first world war. Witnessing the achievements of military medicine, Law decided that if he should ever have the opportunity, a monument would be created in oils honoring American medical pioneers. Five years ago, at his behest, Wyeth commissioned the American artist, Dean Cornwell, to begin such a series.

PAST YEAR'S U. S. P. ACTIVITIES ANNOUNCED

SPANISH TRANSLATION READY. PHARMACISTS ASKED TO SEND FOR FIRST BOUND SUPPLEMENT. PREPARE NEW M. P. REFERENCES

AT THE meeting of the U. S. P. Board of Trustees in New York, Dr. E. F. Kelly, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, was reelected chairman of the Board, and Dr. Adley B. Nichols of the Philadelphia College of Pharmacy and Science was reëlected secretary.

The business of the U. S. P. Board during the past year was conducted through 40 of the customary Board Letters, which covered almost 700 items. An announcement from Dr. Nichols summarizes the principal activities.

Due to the increased tempo of U. S. P. revision, particularly through the demands of the various governmental war agencies and because of changes caused by shortage of critical materials, the Board of Trustees authorized the immediate preparation of the First U. S. P. XII Bound Supplement. Work on this Supplement has been pushed energetically by the Committee of Revision. To aid in obtaining the widest possible cooperation from all interested parties, the Board authorized the holding of an open hearing in New York City, where all proposed texts could be freely discussed. So many questions and problems were raised at this hearing that the Committee of Revision has been extremely busy trying to settle the various questions so that the Supplement may make its appearance at the earliest possible date.

Every owner of a U. S. P. XII is entitled to a copy of this Supplement, as indicated by the post card order form which will be found attached to the inside of the back cover of each U. S. P. The owner should insert the coupon number of his U. S. P. XII (see reverse of U. S. P. title page) his printed name and address, and his signature, and mail the card, which is self-addressed. The Bound Supplement will then be sent as soon as it is available.

During the course of the year the Board authorized the purchase of additional stocks of some

reference standards and also authorized the establishment of certain new reference standards. A new class of reference standards has been approved for the purpose of providing typical melting-point references This new series is not yet available, although work on them is progressing, and it is expected that they will be announced in the near future.

The Board announces that the sale of the U. S. P. XII has practically paralleled that of the U. S. P. XI, slightly exceeding that of the latter for the first year. Under the present conditions there was naturally some misapprehension as to possible demands for the new volume, and it is encouraging that distribution has not been materially hampered.

Spanish Translation

Translation of the U. S. P. XII into Spanish has been completed, and final copy of the First Bound Supplement for U. S. P. XII is now being awaited, since it will be translated and incorporated into the Spanish edition. At its recent meeting, the Board considered bids for the distribution and sale of the coming Spanish edition of the U. S. P. XII, and awarded the contract to the University Society, Inc., of 468 Fourth Avenue, New York City. The University Society are educational publishers with branch offices and agents in many of the Latin-American countries. It is expected that the present friendly relationship being developed between the Americas will materially advance the interest in the Spanish edition of the U. S. P.

The Board is arranging for the publication of a bound Spanish edition of the Second Series, Pharmacopœia and Physician Articles, the popular and authoritative articles which originally appeared in the *Journal of the American Medical Association*. The first series was likewise published in Spanish and was distributed rather extensively.

At the time of the appearance of the new U. S. P. XII, the Board authorized the issuance of a letter under the signature of Dr. Cary Eggleston, president of the Convention, to the various national, state and county medical associations and societies, calling attention to the new Pharmacopœia and urging the associations to arrange programs to acquaint their members with the new features of the book. Enclosed with Dr. Eggleston's letter was a copy of "What's New in the U. S. P.," a small pamphlet résumé of the new additions to the U. S. P., as originally prepared for distribution at the convention of the American Medical Association. Included also was a reprint of an article by Tice and Smith, as prepared for the Second Pharmacopœia and Physician series. This article reviewed the new U. S. P. in more detail, devoting particular attention to the new admissions, their characteristics, use, and similar pertinent information.

Reprints of an article by Eggleston and Gold entitled "Progressive Therapeutics as Aided by the U. S. Pharmacopœia XII" (*Am. J. Med. Sci.*, 204 (Nov. 1942), 757) were also made available for distribution during the year. This article was of particular interest to the medical profession, and presented a résumé of U. S. P. XII items classified therapeutically.

The Board is working on a plan for further distribution of literature of this nature, both to physicians and to pharmacists, the new material to include data from the coming First Bound Supplement to the U. S. P. XII. A study of such material provides both the physician and the pharmacist an opportunity to keep up-to-date with the new standards.

During the past year the proceedings of the adjourned meeting of the U. S. Pharmacopœial Convention, held at Cleveland in 1942, were distributed. The Cleveland Meeting was held to receive the report of the special committee on the revision of the constitution and by-laws of the Convention. Numerous by-laws were changed and suggestions made for further changes, both to the by-laws and to the constitution, the latter action to be taken at the time of the 1950 Convention.

Baby Week, designated as Nov. 8 to 15, may well mark an increased demand for infants' health needs, for an extra dividend of 2,000,000 babies will have come to the nation in the decade since 1933. Statisticians arrived at this figure by using the 1933 birth rate as the standard.

REFRIGERATION GIVES

Better Syrup of Orange

POPULAR VEHICLE IMPROVED BY PREPARING AND STORING SYRUP UNDER REFRIGERATION

by W. H. GLOVER, L. M. OHMART, and M. J. STOKLOSA

MASSACHUSETTS COLLEGE OF PHARMACY

ALTHOUGH prescription surveys reveal that Syrup of Orange, U. S. P., is one of the most frequently used of the syrup vehicles, it is the opinion of the authors that the syrup of orange commonly dispensed does not fully represent the possibilities of the official preparation.

When first prepared, Syrup of Orange is a brilliant, golden-yellow syrup with the delicate and refreshing fragrance and taste of fresh, ripe oranges. Under the conditions of storage recommended by the Pharmacopœia and followed in most prescription departments, the appearance, taste and odor of the syrup change rapidly. Within a period of a few days, at most, the syrup begins to lose some of its brilliancy and the taste and odor have undergone such marked changes that they are only faintly reminiscent of fresh oranges. While these changes are probably too subtle to be demonstrated chemically, they are perfectly apparent to the senses and detract seriously from the usefulness of Syrup of Orange as a prescription vehicle.

Acting on the theory that the undesirable changes which take place in Syrup of Orange are due to the conditions under which the preparation is usually stored, a study was undertaken to determine if storage at a low temperature would retard these changes.

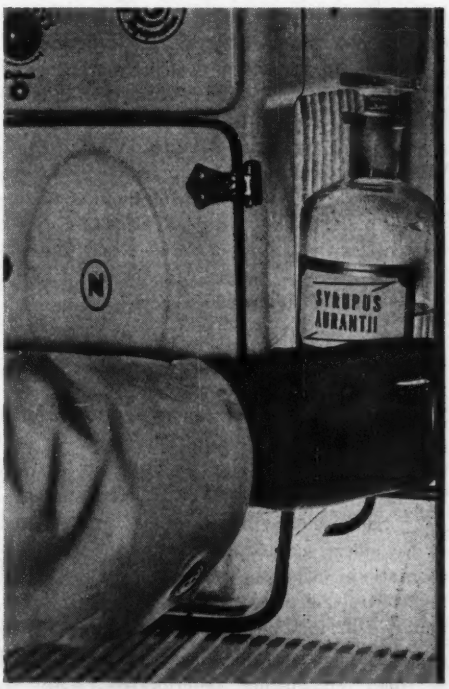
Experimental

Four series of samples of Syrup of Orange were prepared.

Series 1.—Three 500-cc. samples were prepared by the official method and were stored at room temperature during the observation period of four months.

Series 2.—Three 500-cc. samples were prepared by the official method. Immediately following their completion, they were placed in a mechanical refrigerator at a temperature of 2° C. and were maintained at approximately that temperature during the observation period.

Series 3.—Three 500-cc. samples were pre-



pared by a slight modification of the official method. The modification consisted of adding sucrose to the clear filtrate and placing the product under refrigeration at once, before solution of the sucrose. It was found impossible, without elevating the temperature, to dissolve completely the sucrose by this method. The amount remaining undissolved, however, was so slight as to be considered negligible.

Series 4.—Five hundred cubic centimeters of Tincture of Sweet Orange Peel were prepared by the official method, except that the maceration and filtration were carried out under refrigeration. From the tincture so prepared, three 500-cc. samples of Syrup of Orange were prepared by the official method, modified by conducting the entire process within the refrigerator. The samples so prepared remained under refrigeration during the observation period of four months. As in Series 3, there was a negligible amount of sucrose remaining undissolved.

At intervals of two weeks, during the observation period, the samples of the several series were examined for brilliance, odor and taste. The samples of Series 1 showed a rapid deterioration in these respects and at the end of one month, showed little resemblance to the original products. At the end of the observation period of four months, the samples of Series 2, Series 3 and Series 4 showed little or no change in their original brilliancy, flavor and odor. Although the differences among the samples of these three series were not great, it is the opinion of the investigators that the flavor and odor of Series 3 were better than those of Series 2 and that the samples of Series 4 were superior in these respects to those of Series 2 and Series 3.

Summary

1. Syrup of Orange, when prepared and stored according to the official directions, rapidly undergoes deterioration, losing its brilliancy and its characteristic odor and taste of fresh oranges.

2. Samples of Syrup of Orange were prepared by the official method modified by the use of refrigeration. All of the samples except those used for control purposes were stored at approximately 2° C. for a period of four months.

3. The control samples, prepared and stored at room temperature, deteriorated rapidly in clarity, flavor and odor. The samples which were prepared and stored under refrigeration showed no impairment of clarity, flavor and odor during the observation period of four months.

Presented by title to Section on Practical Pharmacy, A. PH. A., Columbus meeting, 1943.

PROPYLENE GLYCOL MAKES QUINIDINE INJECTABLE

by HARRY BRASS, Chief Pharmacist
BETH ISRAEL HOSPITAL, BOSTON

THE medical profession has been in need of an injectable quinidine preparation in a concentration such that each cubic centimeter is equivalent to two to three grains of quinidine. Such a preparation has been discussed by Sturnick, Riseman and Sagall (*J. A. M. A.*, 121:917, 1943). Another approach was suggested a year ago by Dr. Mark D. Altschle of our medical research laboratories, that is, that propylene glycol might prove a useful vehicle for this purpose. The author has found this to be true, using the following formula:

Quinidine hydrochloride	10.0 gm.
Propylene glycol	75.0 cc.

The quinidine hydrochloride is placed in a suitable container and enough propylene glycol added to make 75.0 cc.; on application of heat the quinidine hydrochloride readily goes into solution. When the mixture is cool, sufficient propylene glycol is added to make 75.0 cc.

This solution is put into ampuls and sealed. It is neither filtered nor autoclaved. Cultures were made from such ampuls and reported as negative. The solution did not show discoloration or crystallization over a period of more than six months. Studies are now in progress relative to the stability of more concentrated solutions of quinidine in propylene glycol.

When this preparation is given intramuscularly in man, evidence of the action of quinidine is detectable in fifteen minutes and persists for approximately two hours. Although safe for intramuscular injection, the solution should not be given intravenously.

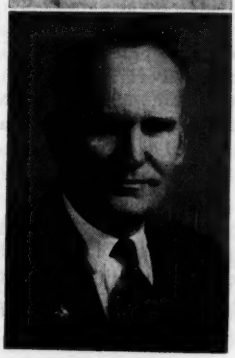
INTRODUCING

A. PH. A. PRESIDENTIAL NOMINEES

BALLOTS for the election of 1944–1945 officers of the AMERICAN PHARMACEUTICAL ASSOCATION have now been mailed. Brief biographical sketches of the presidential candidates, nominated by the House of Delegates at the Columbus meeting, are presented to aid members in casting their ballots. Every member is urged to vote, for the selection of officers to guide the wartime activities of the ASSOCIATION is of importance to every pharmacist. The bylaws provide that only those ballots received within 30 days of the date printed on the ballot will be counted.

Paul G. Stodghill. Born at Salida, Col., in 1898, Mr. Stodghill entered pharmacy as an apprentice when only 14 years old. He left the profession temporarily to serve in the armed forces during World War I, and after discharge continued to serve in the Army Reserve Corps until 1933. The ethical prescription pharmacy which he operates was opened in 1922. Long active in association work, Mr. Stodghill has been 2nd vice-president, 1st vice-president and president of the Colorado Pharmacal Association, as well as chairman of the executive committee. He is now 1st vice-president of the AMERICAN PHARMACEUTICAL ASSOCIATION, and 1st vice-president-elect of the American College of Apothecaries, an organization which he helped to found. Mr. Stodghill lives in Denver with his wife and daughter, where he is active in community affairs. He is a member of the local Chamber of Commerce, Denver Gyro Club, Denver Exchange Club, Ad Am An Club and Phi Delta Chi fraternity.

George A. Moulton. After graduation from the Massachusetts College of Pharmacy, Mr. Moulton opened the professional pharmacy in Peterborough, N. H., which he and his pharmacist-wife have operated since. As a member of the New Hampshire Commission of Pharmacy for the past 10 years, and its present chairman, he has been the author of much pharmaceutical legislation. He is past-president of the N. A. B. P., member of the National Syllabus Committee, voting delegate from the N. A. B. P. to the 12th Revision Convention of the U. S. P. and 2nd vice-president of the Convention. He is on the national legislative committee of the N. A. R. D., a vice-president of the National Secretary's Conference, a member of the A. PH. A. House of Delegates for the past 10 years and a 2nd vice-president. As past-president of the New Hampshire Association and its present executive secretary, he has been editor of its annual year book and originator of the New Hampshire Plan of state association organization.



M. Nile Ford. A native Ohian, born in 1882, Mr. Ford's early college training was obtained at Ohio Northern University. He later entered Scio College of Pharmacy, and upon completing the course in 1905 was awarded the prize for pharmaceutical laboratory work—a membership in A. PH. A. After holding positions as retail pharmacist and manufacturing pharmacist, Mr. Ford was named secretary of the Ohio Board of Pharmacy in 1912. He has held this position ever since, being active in national as well as state pharmaceutical affairs. Official posts have included the presidency of the N. A. B. P., past-chairman of the A. PH. A. House of Delegates, member of the Pharmaceutical Syllabus Committee, secretary of the Conference of Pharmaceutical Law Enforcement Officials and delegate from the Ohio Association to the last three U. S. P. Conventions. He is affiliated with all national, state and local pharmaceutical associations, and is a Knight Templar, 32nd degree Mason and Shrine member.

A. S. H. P. HOLDS INAUGURAL MEETING

FIRST SESSION OF ORGANIZED HOSPITAL PHARMACY HELD AT NINETY-FIRST A. PH. A. MEETING; CHAIRMAN OUTLINES PROBLEMS

THE American Society of Hospital Pharmacists, one of the most professionally minded but newest groups in pharmacy, held its first annual meting in Columbus in conjunction with its 90-year-old parent organization, the AMERICAN PHARMACEUTICAL ASSOCIATION.

About 70 charter members convened to hear Chairman H. A. K. Whitney's opening address. In the absence of Mr. Whitney due to illness, the address was read by his colleague, Don E. Francke of University Hospital, Ann Arbor, Mich.

Pointing out that the new organization must hack, scratch and build a pathway through uncharted areas and imposing obstacles, Mr. Whitney declared that "Whatever detailed course we choose to follow, let magnanimity and altruism be our guide, for if we should be labeled personal and selfish much effort will be sterile."

Seven subjects were enumerated which demand the consideration of the hospital pharmacists and the choice of a course of action:

1. Shall we continue the fight for a uniformly acceptable system of collegiate training?

2. Shall we ask for an amplification of present curricula, revising them so our general education in the liberal arts is increased, our professional education to include more subjects designed to bring us closer and of more assistance to the medical profession and its work?

3. Shall we not develop a research spirit by revising our own practices and actively engage in an evaluation, or reëvaluation, of the tools, methods and end products with which we are in daily contact—our materia medica?

4. Shall we attempt to determine the absolute minimum rquirement for postgraduate experience (if this be the method of approach) for the special practice of hospital pharmacy? This may involve the source of this experience (qualitative); the time element involved (quantitative); and a recognition of such suitable, supervised experience by an award of generally acceptable recognition or certification (academic).

5. Shall we seek national recognition (registration), permitting practice in any state of the Union, by proposing a minimum of educational and experience qualifications for all states to follow, thus raising the professional levels for all practicing pharmacists?

6. Shall we express our thoughts on the subject of using present facilities for post-war health services, or should the establishment and expansion of health centers (possibly under Federal control) be encouraged? Or, perhaps, there may be a happy medium combining the two projects.

7. Do we have any feelings on the presumed encroachment of monopolistic (*sic!*) elements in the larger sphere of the drug "industry" of manufacturing and distribution? Simple practices in pharmacy are now reserved for the hospital pharmacist, but, where do the simple practices end and the more complex practices begin? If one, by schooling, does acquire certain abilities for the "more complex" practices then how to extend them? And lastly, might not the 90-day "pharmacists" be held as sufficient for the "simple" practices?

The professional level at which the hospital pharmacists are aiming is indicated in this A. S. H. P. resolution which was submitted later to the A. PH. A. Long Range Program Committee for recommendation:

The institution of a period of not less than one year of hospital pharmacy interneships for qualified graduates who have completed a hospital pharmacy course in an accredited school of pharmacy,

That such interneships be spent in hospitals approved by the American College of Surgeons and approved by the American Medical Association as meeting the requirements for interneships for the medical sciences and public health services,

And that such hospitals meet the minimum standards for a hospital pharmacy service as defined by the American College of Surgeons and, further, that the services of the American College of Surgeons, the American Hospital Association and the American Society of Hospital Pharmacists be coöperatively used to survey the hospitals making claim to such standards for the purpose of determining fitness,

Also that an outline of the principles of such a hospital pharmacy interneship be prepared by a committee appointed by the chairman of the American Society of Hospital Pharmacists and that same, when completed, be submitted to the American Association of Colleges of Pharmacy for criticism and suggestions.

And lastly, that such hospital pharmacy interneships be accepted by all-examining boards of pharmacy as a prerequisite of experience toward the examination of the candidate for license.

New officers elected for 1944 to handle the rapidly expanding activities of the A. S. H. P. are: *chairman*, Don E. Francke, University Hospital, Ann Arbor, Mich.; *vice-chairman*, Hazel E. Landeen, 1313 East Ann Street, Ann Arbor, Mich.; *secretary*, I. Thomas Reamer, Duke University Hospital, Durham, N. C.; *treasurer*, Sister Mary John, Mercy Hospital, Toledo, Ohio.

NEW EDITOR APPOINTED FOR JOURNAL

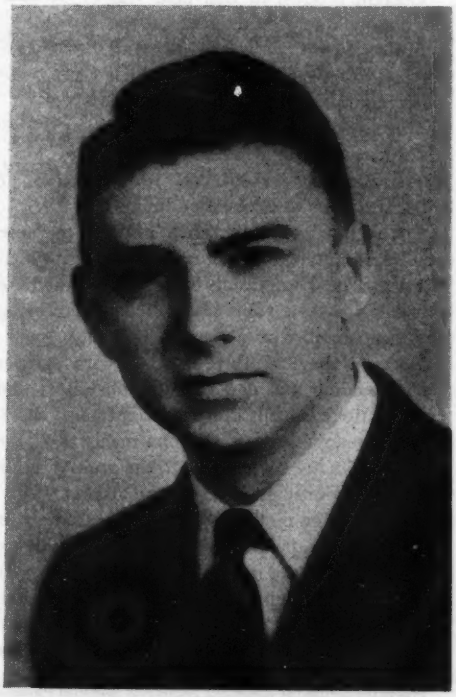
WITH the current issue of THIS JOURNAL, Glenn Sonnedecker assumes the editorship, replacing Robert W. Rodman, who has resigned to become an account executive for Murray Breese and Associates, New York.

Mr. Sonnedecker, a pharmacist-writer, has been on the editorial staff of Science Service, Washington, D. C., for the past year-and-a-half. His articles on pharmacy and the allied sciences have been syndicated widely for use by newspapers, magazines and radio.

The new editor is registered with the Ohio board, and has had practical experience in retail pharmacy. He is a graduate of Ohio State University Pharmacy College, where he also took special studies in journalism. Affiliations include A. PH. A., Phi Delta Chi, Phi Rho Alpha, Sigma Delta Chi, and the American Association of Scientific Workers.

THIS JOURNAL, now nearing its fourth birthday, has had two former editors. When the old JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION was split into the Scientific and Practical Pharmacy editions, Dr. E. F. Kelly, secretary of the ASSOCIATION, launched the latter publication in a temporary capacity.

A year later in January, 1941, Robert W. Rodman, then of *Druggists Circular*, was appointed the first full-time editor. Since then THIS JOURNAL has been developed, not only as an organ of the ASSOCIATION, but as a useful professional journal for every retail and hospital pharmacist.



GLENN SONNEDECKER

Which Ointment Base?

EFFECT OF OINTMENT BASES ON ANTISEPTIC POWER AND ABSORPTION IS EVALUATED. NEARLY UNIVERSAL ATTEMPT TO GET A UNIVERSAL BASE

by L. W. BUSSE
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WIDE diversity of opinion as to the value of the ointment bases developed up to the present is revealed by a review of the literature. A universal attempt to find a universal ointment base can be discerned. The U. S. P. XII has apparently adopted such a policy by making either Ungentum Alba or Unguentum Flava the base for most ointments contained therein.

Current interest in this field was no doubt largely stimulated by the "implantation" technique and methods for absorption studies which this technique made possible. Also, the intense desire to achieve systemic absorption through cutaneous administration of substances, which otherwise were of necessity administered by injection, gave great impetus to these studies. Introduction of substances from which the degree of absorption is measured by a definite physiological end point also aided in increasing the great number of workers in this field.

Because the literature abounds with articles recommending and condemning substances and combinations of substances as ointment bases, the pharmacy student, the pharmacist and the medical man are confused as to the true value of the various ointment bases on the market.

In evaluating ointment bases we must keep in mind the therapeutic objective to be achieved from the substance incorporated in the base. In an analysis of substances administered in this way there appear to be three general objectives which a physician desires to achieve: (1) local emollient or irritant action; (2) local antiseptic action; (3) systemic absorption. There do not appear to be any scientific methods of measuring local emollient action, and therefore little scientific material can be quoted as to the value of the various bases for this effect The second and third objectives, however, offer means of scientific study and logically therefore most of the literature pertains to the action of the bases in achieving either of these objectives.

The study of the effect of vehicles on the antiseptic efficiency of various substances was apparently initiated by Koch,[1] when he advanced the theory that when phenol is dissolved in oil or alcohol it shows no antiseptic properties. Since then, many workers have substantiated this statement as regards phenol in oil or oily bases. Reddish and Wales,[2] Gershenfeld and Miller,[3] Prout, Eddleman and Harris,[4] Burnside and Keuver[5], Craw and Lee,[6] Foley and Lee[7]—all have shown that phenol when incorporated in various greasy bases in 2% concentration is not bactericidal in action. Bryan[8] found that at least 10% of phenol was necessary to produce bactericidal potency when incorporated in greasy bases. This was subsequently confirmed by Clark[9] in 1939 when in a series of tests he showed that a 10% phenol ointment in petrolatum failed to produce a measurable zone of inhibition on a 10% serum agar plate.

Since 1933 when Gershenfeld and Miller[10] showed the increased effectiveness of 2% phenol ointments and other phenolic compounds in water-miscible bases over that of greasy bases, many of the above workers have confirmed their results. The following table from Burnside and Kuever[5] in 1940, for example, shows the effectiveness of various phenolic-type ointments with a proposed emulsion ointment base.

Presented before the American Society of Hospital Pharmacists, A. Ph. A. meeting, Columbus, Ohio, 1943.

	Per Cent	pH	Zone Mm.
Hexylresorcinol	2	4.8	12
Chlorthymol	2	5.1	8
Chlorcarvacrol	2	4.6	7
Thymol	2	5.0	7
m-Hydroxy diphenyl	2	4.9	7
Phenol	2	4.6	6
Betanaphthol	2	4.8	6
3-Chlor-4-hydroxy diphenyl	2	4.8	3
o-Hydroxy diphenyl	2	5.2	4
Resorcinol	2	4.9	3
p-Hydroxy diphenyl	2	5.2	2.5
Trinitrophenol	2	Acid	1

Ointment	Official Base	S. H. C. O.	"Cream Base" 40% H_2O
Ammon. mercury	7	14–15	15–16
Boric acid	0	4	6
Calomel	2.5	3	6
Calomel, colloidal	4–6	4–5	6
Iodine	18	28	...
Phenol	0	0–2	1–2
Pine tar	3–4	4–5	7–8
Red mercuric oxide	5–6	9–11	10
Yellow mercuric oxide	4–5	14–15	8–10
Whitfield	11–12	10–12	15
Whitfield, half-strength	8–9	7–9	13
Proprietary A	7–8	9–10	...
Proprietary B	3–4	5–7	9–10

Gershenfeld and Brillhart[11] in 1939 also showed the increased effectiveness of ammoniated mercury, phenol and bichloride of mercury in ointment bases containing water as an o/w emulsion. On the basis of these results, he proposed the following classification of ointment base groups according to the size of the zone of inhibition: (*a*) synthetic wax base, (*b*) oxycholesterin, (*c*) benzoinated lard, (*d*) U. S. P. XI ointment, (*e*) petrolatum base.

Fiero and Loomis[12] in 1942 also reported the increased effectiveness of antiseptics, including phenol in 2% concentrations, when incorporated in sulfated hydrogenated castor oil and a "cream base" containing 40% of water. The following table of their results is expressed in millimeters of antiseptic zone surrounding the ointment.

In summarizing they state, "Bacteriological tests indicate that the antiseptic value of these ointments is equal to, or superior to, the official ointments."

A careful examination of the results in the above table does not substantiate entirely the claim for emulsion bases as vehicles for antiseptics. Colloidal calomel, iodine proprietary "A" and yellow mercuric oxide either showed insignificant increases in effectiveness, decreased effectiveness over anhydrous preparations, or lost their activity entirely.

Foley and Lee[7] in 1942 also carried out an interesting series of tests on a number of vehicles and their results again do not entirely support the claim for water-containing bases as carriers for antiseptics. The table of their results below is for ointments of official strength.

	Boric Acid, Mm.[a]	Ammoniated Mercury, Mm.	Yellow Oxide Mercury, Mm.	Calomel, Mm.	Phenol, Mm.	Iodine, Mm.	Whitfield, Mm.	Ichthammol Mm.	Calamine, Mm.	Zinc Oxide, Mm.
U. S. P. ointment	..[b]	6	5	0	..	10	0	0	0	..
N. F. ointment	0[c]	0	0	3	0	0	4	3	3	..
Petrolatum	..	5	5	1	..	10	4	3	..	..
Hydrous wool fat	..	7	5	3	..	15	6	3	1	..
Anhydrous wool fat	..	6	4	3	..	14	6	2	..	..
Aquaphor	..	6	5	1	..	20	4	0	..	..
Aquaphor; Water *aa*	4	6	5	3	..	1[d]	71	4	..	..
Base 37	..	6	5	1	..	15	4	0	3	..
Base 37; Water *aa*	4	6	5	3	..	1	7	4	5	..
Neutramul	0	6	6	0	..	1	0	0	0	..
Neutramul; Water *aa*	0	6	6	0	0	1	0	0	0	..
Gardinol base	0	6	0	0	..	0	0	0	0	..
133 T (Goldschmidt Corp.)	0	0	5	0	1	0	0	4	..	..
Seltzer base 4-Water *aa*	0	0	0	0	4	0	0	0	0	..
Vanishing cream[e]	5	10	8	4	3	1	7	4	2	2
Sodium alginate 5%[e]	9	0	8	4	2	1	1	1	2	2
Methyl cellulose 1500, 5%[e]	9	6	8	4	0	1	1	1	2	2
Methyl cellulose 1500 15%[e]	0	6	0	3	3	1	0	1	0	0

[a] Width of zones of inhibition in millimeters; [b] negative results; [c] no test made; [d] incompatibility; [e] controls showed zones of inhibition of 1 to 2 mm.

"At first glance," they conclude, "the results of this study would seem to present a good case in favor of the water-holding bases as vehicles for antiseptic chemicals. Upon closer examination, it will be observed that ammoniated mercury, yellow oxide of mercury, calomel, iodine, benzoic and salicylic acids, ichthammol and even prepared calamine were all bacteriostatic as official ointments. The antiseptic action of each was not greatly accelerated when incorporated in the water-holding bases such as aquaphor, Base 37, Neutramul and similar products."

One of the most interesting studies was that carried out by Clark[9] in 1939 on the antiseptic value of certain phenolic ointments. These experiments, shown in the table at the right, were made under the following test conditions:

Ointments were prepared using prolonged fusion and aged two months or more. F. D. A. serum agar plate method was used and incubated at 370° C. for 24 hours. The test organism was *Staphylococcus aureus A 209*. (*See table.*)

Effect of Age

Clark states in regard to the vanishing cream bases that "When first tested these ointments gave better zones than any reported so far in this paper. However, considering the manufacturing technique it was decided to age these samples in a warm place for several hours. The final zones were: 2% phenol, barely discernible; 5% phenol, 4 mm.; 10% phenol, 7 mm; 2% parachlor meta xylenol, very small; 2% chlorthymol, partial inhibition; and 2% paraamylphenol, very small."

Clark also states, "The original zones were very large." Yet when these ointments of phenolic substances were aged for two months they exhibited no bacteriostatic effect and the zone of inhibition for phenol itself was only 1 to 2 mm. "Another important fact to be kept in mind," he concludes, "is that a freshly prepared ointment which has had little or no fusion may be decidedly antiseptic for a short time and the antiseptic value gradually diminished. This fact may account for variations reported by different investigators using the same formula. Before any phenolic ointment is declared antiseptic, it should be aged sufficiently to indicate that the antiseptic power will not disappear in time."

Base	*Petrolatum*	*Petrolatum and 5% Wax*	*Petrolatum, 2% Sodium Lauryl-Sulfonate, 5% Glycerin*	*Petrolatum, 2% Sodium Lauryl-Sulfonate, 2.5% Glycerin, 2.5% Water*	*Petrolatum, 2% Sodium Lauryl-Sulfonate, 2.5% Glycerin, 2.5% Water, 1% Thymol*	*Wool Fat, Anhydrous*	*Wool Fat, Hydrous*	*Cocoanut Oil, Petrolatum, 50–50*	*Crisco*	*Spry*	*Vanishing Cream, A. Ph. A. Recipe Book*
Phenol 2%	No zone	.....	.....	No zone	Small zone of partial	.....	No zone	.....	.....	.....	1–2-Mm. zone
Phenol 5%	Too small	.....	No zone	1/2–3/4-Mm. zone	1.5-Mm. zone	.....	1/2-Mm. zone	No zone	No zone	No zone	4-Mm. zone
Phenol 10%	Too small	1.5-Mm. zone	2-Mm. zone	3/4-Mm. zone	1.5–2-Mm. zone	4-Mm. zone	5-Mm. zone	No zone	7-Mm. zone	7-Mm. zone	7-Mm. zone
Paraamyl 1% phenol	No zone	.....	.....	1/2-Mm. zone	1/2–1/4-Mm. zone	.....	.....	.....	.....	.....	.....
Paraamyl 2% phenol	Only partial inhibition	Well defined but too small	1.5-Mm. zone	1-Mm. zone	2–3-Mm. zone	No zone	No zone	No zone	No zone	No zone	Too small
Paraphenyl 1% phenol	.....	.....	.....	.....	Partial only	.....	.....	.....	.....	.....	.....
Paraphenyl 2% phenol	No zone	Too small	2-Mm. zone	1.5-Mm. zone	2–3-Mm. zone	No zone	No zone	No zone	No zone	No zone	No zone
Parachlor metaxylenol 1%	1.5-Mm. zone	.....	.....	3-Mm. zone	Partial only	.....	.....	.....	.....	.....	.....
Parachlor metaxylenol 2%	3+-Mm. zone	2.5-Mm. zone	3 1/2–4-Mm. zone	4–5-Mm. zone	(5-Mm. partial) 3-Mm. zone	No zone	No zone	No zone	No zone	No zone	Too small
Thymol 2%	Only partial inhibition	Too small	Small, erratic	Only partial inhibition	.....	No zone	No zone	No zone	No zone	No zone	Only partial
Chlorthymol 1%	No zone	.....	.....	1–2-Mm. zone	.....	.....	No zone	.....	.....	.....	.....
Chlorthymol 2%	1-Mm. zone	Too small	1–2-Mm. zone	3-Mm. zone	2.5-Mm. zone	No zone	No zone	No zone	No zone	No zone	Too small
Santophen "7" 2%	1.5-Mm. zone	1.5-Mm. zone	1-Mm. zone	1.5-Mm. zone	2–3-Mm. zone	No zone	No zone	No zone	No zone	No zone	No zone

In summarizing and analyzing results reported on antiseptics incorporated in these various types of bases, only general conclusions can be made:

1. There is as yet no ointment base reported which can serve as a universal ointment base.
2. The conclusion of G. F. Reddish "that the antiseptic value of an ointment could not be told by the antiseptic value of its constituents," still holds true.
3. The claims for water-containing ointment bases as vehicles for antiseptics over the greasy type bases are not justified, except on an individual basis.
4. The chemical and physical nature of the antiseptic which is incorporated in the base has as much as or perhaps more to do in determining the final bactericidal action of the product than the composition of the vehicle in which it has been incorporated.
5. Tests to determine the antiseptic efficiency of a substance when incorporated in an ointment type vehicle should be determined on so-called "aged" ointments to get a true test of the value of the base.

Systemic Absorption

A review of the reports pertaining to the absorption of substances through the skin again reveals a wide diversity of opinion, both as to mechanism of absorption and the influence on absorption of the various substances used as ointment vehicles.

Analysis of the reports on the various theories advanced as to the mechanism of absorption of substances incorporated in ointment bases seems to reveal a majority of evidence in favor of absorption taking place via the hair follicles, along the hair shafts and into the oil gland ducts.[13, 14, 15]

Some of the more interesting theories were advanced by Kionka[16] in 1931 who regarded the epidermis as a cellular membrane saturated with fats containing cholesterol and believed that only substances soluble in these fats could diffuse through the epidermis. He also postulated that the base in which the medicament was applied influenced the rate and degree of absorption. Brown and Scott[17] in 1939 indicated a substance must possess both oil and aqueous solubility in order to penetrate the human skin and that "an extremely high or low partition coefficient is less conducive to absorption than intermediate values." They found that the type of base had no effect on the quantity of substance absorbed.

This substantiates Sollman's[18] work in 1918 when he stated that oils and ointments delay the absorption of fat-soluble substances, such as phenol, mustard oil or dichlordiethyl sulfide, analogous to the partition of a substance between a good solvent and a poor solvent in a test tube. Sauerland[19] in 1912 also concluded that the influence of the ointment base varies according to the substance.

Starkenstein and Hendrych,[20] in 1936, attributed to cholesterol a penetrability-regulating action and concluded that it must exercise a protective action since an insulin ointment which failed to produce any blood sugar lowering when rubbed on the normal skin of a rabbit, produced a startling drop in blood sugar level if the skin was previously washed with petroleum ether, a solvent for cholesterol.

One of the most interesting experiments along this line was carried out by Kahlenberg[21] in 1924. He tested the absorption of solutions of boric acid, lithium chloride, rubidium chloride, cesium chloride, strontium chloride, lithium perborate and sodium perborate by immersing the feet to a depth just above the ankle in the solution to be tested. Samples of urine were taken from time to time and analyzed. It was found that free boric acid alone passed through the living skin in perceptible quantities.

He postulated, "The solution of the latter (boric acid) probably is adsorbed by the skin, loosely combined with the latter, and from this loose combination the boric acid is swept away by the blood stream." All of these substances however, passed readily through the dead human skin and through other dead animal membranes. Kahlenberg stated also, that since experiments on osmosis demonstrated conclusively that the chemical nature of the membrane was the factor determining whether a substance would pass through the membrane, he was led to the conclusion that dead skin and living skin were chemically different, for they acted different osmotically.

Bliss in 1934[22] and 1935[23] employing the histology of the skin to explain his conception of absorption, pointed out that the site of application, thinness of the skin, freedom from hair and richly supplied lymphatics were aids for absorption. He also concluded that the drug itself

rather than the vehicle in which it was applied was the determining factor of absorption.

The work of Lasareff, Frussilevskaya and Livschitz[24] in 1931 paved the way for some of the more recent experiments. They found that solvents such as benzene, ether and acetone were themselves absorbed into the blood stream when inuncted on the ear of a rabbit, or on the human skin. They suggested that these solvents might therefore carry a dissolved hormone with them.

Zondek[25] in 1929 showed that oestrone was absorbed by the skin. He found that seven times the amount which produced vaginal cornification by injection was necessary to do so by inunction with the hormone when incorporated in oil or ointment, to the shaved skin of mice.

Emmens[26] in 1940 stated that the volatile organic solvents—ether, benzene and 96% alcohol —were more effective carriers of active material from the skin surface than was nut oil or lanolin. In his experiments with rats and mice, inunction in benzene or ether was as effective as, or even more effective than, injection of the same medicament dissolved in oil. In tests with rabbits inunction in benzene, but not in ether, was superior to injection in oil. He also postulates a slight but consistent superiority of ether as a medium for inunction of estrogens and of benzene for inunction of androgens.

Macht[27] in 1938 reported on the relative penetration of fats and oils through the skin of animals, particularly rabbits and guinea pigs. *Ointments* were made of petrolatum, lard, hydrous wool fat, a synthetic proprietary preparation of cholesterol, goose fat, bear fat and greaseless creams. *Lotions* were prepared of olive oil, cottonseed oil, mineral oil and peach kernel oil. The penetration of several potent drugs such as nicotine and strychnine incorporated in these bases or vehicles was studied pharmacologically. These experiments revealed that none of the fixed fats carrying potent drugs were absorbed readily, but signs of poisoning developed in some cases only after repeated application of the ointment for several days. Hydrous wool fat was more efficient than the other fats, but on the whole the results obtained with drugs incorporated in fats as well as in olive oil, linseed oil and liquid petrolatum were disappointing. Some drugs incorporated in fats were absorbed less readily than the same drugs applied in aqueous or hydro-alcoholic solution.

A most interesting series of experiments to determine the effect of media on the absorption of drugs was carried out by Fuller, Hawking and Partridge[28, 29] in 1942. This work is significant not only because of its scientific value but because it comes as a joint paper from the National Institute for Medical Research and the Laboratory of the British Pharmacopœia Commission. "Theoretically," they state, "the process of absorption from a sulphonamide preparation or ointment base can be divided into various phases:

"1. In the cases of ointments, etc., sulphonamide molecules reach the interface between the preparation and wound fluid either by solution in the aqueous phase of the ointment base or by passage of solid particles through it.

"2. The sulphonamide becomes dissolved in the stationary layer of wound fluid at the interface.

"3. The sulphonamide is transported into the adjacent fluids and tissues (*a*) by diffusion and (*b*) by currents in the fluid."

Solubility Important

They conclude that studies from an *in vitro* method indicate that the differences in rate and amount of absorption between the different "sulfa" compounds apparently depend on their differences in solubility. The results from an *in vitro* study of the absorption and excretion of these compounds when applied to wounds show a satisfactory agreement between the results of the *in vitro* and *in vivo* studies.

These men also conclude that the consideration of fundamental importance is "the ratio of the surface of the preparation to its volume." If the surface is relatively large as in a thin film the delay from oil preparations is small. This is the case when ointments are smeared over a large surface. These authors summarize by stating, "*In vivo* it was found that when the preparation was spread as a thin film over a surface absorption would occur rapidly from all types of preparation studied; but when the preparation was embedded in the tissues as a compact mass, so that the surface volume ratio was low, absorption of sulphanilamide was much delayed by incorporation in an oily medium and somewhat delayed by incorporation in an oil-in-water emulsion."

In summarizing the results of the experiments cited, several points seem to be significant:

1. The more recent evidence seems to show that ointment bases of any type hinder or delay absorption through the intact epidermis or from mucous surfaces.

2. It is the properties or peculiarities of the active substance incorporated in the base which will determine whether absorption will occur through the skin and which will in part determine the rate of absorption if applied to mucous surfaces.

3. Petroleum ether, benzene and chloroform are efficient solvents in preparing the skin for absorption to take place and they will carry substances dissolved in them through the skin much more efficiently than if these same substances were incorporated in so-called ointment bases.

4. The factor of fundamental importance in determining or regulating the rate of absorption of substances when incorporated in various media and applied to *mucous* surfaces is the "ratio of the surface of the preparation to its volume."

5. The future studies of absorption of effective substances incorporated in ointment bases, especially when applied to mucous surfaces, would more profitably be devoted to prolonging the time of absorption rather than with the intent of hastening the rate of absorption by incorporation in an ointment base.

There is an apparent dearth of clinical evidence or studies in comparison with the numerous *in vitro* studies. This is a great field for coöperative research between the hospital pharmacist and the medical staff.

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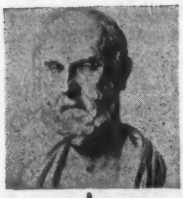
SULFAS STOP RHEUMATIC FEVER RETURN

Authorities at the U. S. Children's Bureau conference on rheumatic fever agreed that the general use of sulfa drugs to prevent repeat attacks of rheumatic fever was justified, a Science Service report to THIS JOURNAL indicates. Of some 700 patients getting sulfa drug prophylactic treatment during the rheumatic fever season, it was reported, only 10 patients had a return of the disease. Among 500 patients not given the sulfa drug prophylaxis, there were 88 repeat attacks. Wider prescribing of sulfanilamide when thus indicated can be expected now that the experimental stage seems to be over.

One of the first physicians to report success in using the sulfanilamide prophylaxis, Lt. Comdr. Alvin F. Coburn, warned the conference against use of the sulfa drugs for minor streptococcus sore throats. In some 40 patients he has seen in the Navy, he stated, he was impressed by the fact that all these patients had their first rheumatic fever attack after being given a sulfa drug for a minor streptococcus throat infection. These men were all over 30 years old, past the usual age for a first attack of rheumatic fever. They had lived where the disease was prevalent and had had similar streptococcus infections before, but escaped rheumatic fever until after they got a sulfa drug for the throat infection.

Comdr. Coburn stated that the reason for this is not known and suggested that further investigations be undertaken to learn more about the mechanism involved.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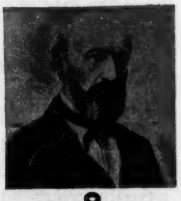
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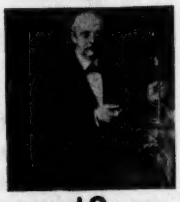
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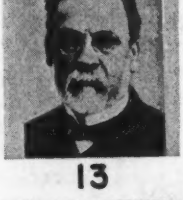
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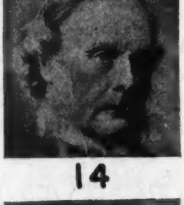
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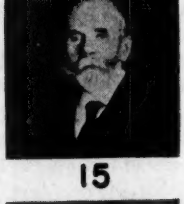
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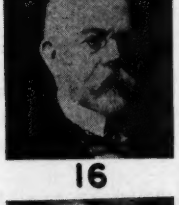
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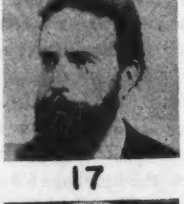
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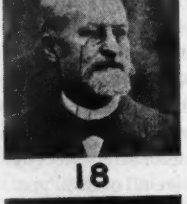
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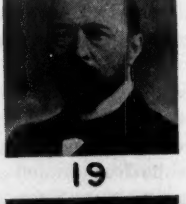
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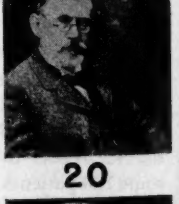
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THE ODD ORIGINS OF MEDICAL DISCOVERIES

by CHARLES WHITEBREAD

ASSOCIATE CURATOR, DIVISION OF MEDICINE AND PUBLIC HEALTH, U. S. NATIONAL MUSEUM

MANY MODERN THERAPIES AND METHODS OF DIAGNOSIS SPRING FROM SUPERSTITIONS OF OLD OR HAVE BEEN ADAPTED FROM DISCOVERIES IN OTHER FIELDS

THE natural desire for self-preservation has led mankind, from earliest times, to accept those things which minister to health and to reject others which are injurious. Believing that folks, who died had committed some error which hastened death, and that those who survived had used certain things not necessary or desirable in health to bring about recovery, man was led to avoid injurious substances, and to adopt remedies and practices which were beneficial and useful.

There are not many substances—animal, vegetable, or mineral—which have not been tried as medicine, and very few new discoveries in other fields escape an early trial for the purpose of ascertaining their possible adaptability for use in the healing art.

Many medical substances and procedures now valuable in the cure and detection of disease, relief of pain, and prolongation of life came into use under very strange circumstances. In fact, medicine is curiously indebted to the nonmedical folks for many of its innovations. This prompted Oliver Wendell Holmes to say:

> "It (medicine) learned from a monk how to use antimony, from a Jesuit how to cure agues, from a friar how to cut for stone, from a soldier how to treat gout, from a sailor how to keep off scurvy, from a postmaster how to sound the Eustachian tube, from a dairy maid how to prevent smallpox, and from an old marketwoman how to catch the itch-insect. It borrowed acupuncture and the moxa from the Japanese heathen, and was taught the use of lobelia by the American savage."

The following are just a few of these odd discoveries:

Ancient Chinese doctors wore fiery red costumes when they visited smallpox patients. They also insisted that the pillows, sheets, and bed coverings be crimson, and that red cloth be suspended from the ceiling to cover the walls of the sick room. This practice spread to many other countries in spite of the fact that it was regarded as sheer superstition. Now the smallpox wards of our modern quarantine hospitals, in the treatment of this disease, use, with full scientific sanction, red and infrared lamps, and windows which permit passage of only red rays. This is done to prevent the skin pustules from forming deep scabs which leave the unsightly pockmarks.

A vague notion among the dairy people of England from time immemorial was that milkmaids were immune to smallpox. Edward Jenner, a medical practitioner of Gloucestershire, was treating a dairy maid. Smallpox was mentioned and the girl said: "I cannot take that disease, for I have had cowpox." This simple statement set Dr. Jenner to work on a series of experiments which popularized vaccination, the practice of giving people the mild disease of cowpox to make them immune to the more virulent disease of smallpox.

Presented by title before the Section on Historical Pharmacy, A. PH. A., Columbus Meeting, 1943.

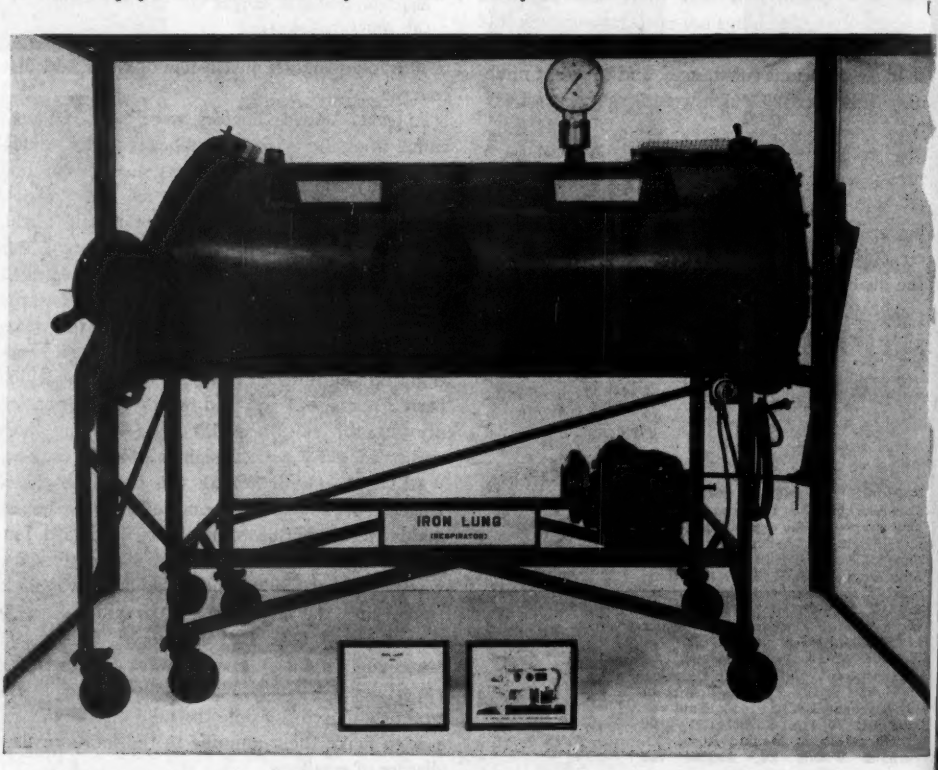
FAMOUS MEDICAL PIONEERS shown in the U. S. National Museum photographs on the opposite page are: 1, Hippocrates; 2, Girolama Fracastoro; 3, Edmund Halley; 4, Leopold Auenbrugger; 5, R. T. H. Laennec; 6, P. C. A. Louis; 7, Richard Bright; 8, C. R. A. Wunderlich; 9, W. T. G. Morton; 10, Florence Nightingale; 11, Rudolf Virchow; 12, H. von Helmholtz, 13, Louis Pasteur; 14, Joseph Lister; 15, Heinrich Quincke; 16, Robert Koch; 17, W. K. Roentgen; 18, Alphonse Laveran; 19, Emil von Behring; 20, Paul Ehrlich; 21, Wm. C. Gorgase; 22, Ronald Ross; 23, Fernald Widal; 24, August von Wassermann.

Crawford W. Long, a pharmacist-physician, who practiced in the state of Georgia, made the following interesting statement concerning how he came to introduce ether as an anaesthetic:

> "On numerous occasions I inhaled ether for its exhilarating effect, and would frequently, at some short time subsequent to its inhalation, discover bruised or painful spots on my person which I had no recollection of causing and which I felt satisfied were received while under the influence of ether. I noticed my friends while etherized received falls and blows which I believed were sufficient to produce pain in a person not in a state of anesthesia, and on questioning them they uniformly assured me that they did not receive the least pain from these accidents. Observing these facts I was led to believe that anesthesia was produced by the inhalation of ether, and that its use would be applicable in surgical operations."

Percussion, an important method of diagnosis in which a physician strikes the body with short, sharp blows as an aid in ascertaining the condition of the parts beneath by the sound obtained, came into use almost two hundred years ago from a very simple observation. Leopold Auenbrugger, the son of an Austrian wine merchant, discovered that he could tell how much wine was left in his father's casks by thumping them with a mallet. If he tapped below the wine level, the sound was dull and muffled. If the cask was tapped above the level of the wine the sound given off was hollow and ringing. After Auenbrugger became a physician he thumped his patients' chests to determine whether the lungs were congested. He passed his knowledge on to his colleagues by means of a book, and the thumping or percussion as it came to be designated, became a standard method of medical diagnostic practice.

For centuries peasants of Central Europe knew that bee keepers did not contract rheumatism, but nothing came of the observation until very recently. Now a preparation made from the stinging apparatus of bees is being used successfully in the treatment of some kinds of arthritis.



IRON LUNGS, developed from this early model, are a life-saving medical contribution from engineering industry.

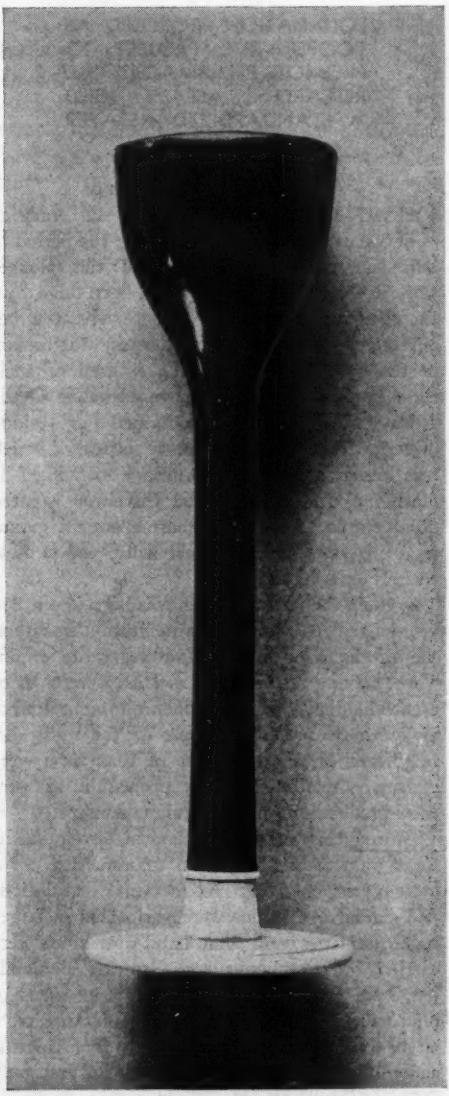
Maggots and snakes were common articles of materia medica in the distant past. First dead maggots were used. Later living maggots were introduced into certain types of wounds so they could live on the diseased tissue thus keeping the wound clean. Now chemical extracts of maggots do the trick. Physicians of old used snakes in their medicines. The venom of poisonous snakes is now collected and used in the development of antivenin. This medicine is made much the same as antidiphtheric serum. First a weak dose of snake venom is introduced into the blood stream of a horse. The strength of the dose is increased until the horse becomes completely immune. The blood serum of the horse then contains antibodies which, when injected into victims of snakebite, quickly gives the immunity which was developed in easy stages in the horse.

Rene Theophile Hyacinthe Laennec, a native of Brittany, a regimental surgeon of the French Revolution, made his name immortal by the invention of the stethoscope. In 1816, wishing to listen to an obese girl's heart, this famous doctor recalled a well-known acoustic phenomenon, namely, if you place your ear against one end of a wooden beam the scratch of a pin at the other extremity is most distinctly audible. He took a piece of paper, rolled it into a very tight roll, one end of which he placed over the heart, and put his ear to the other. He was surprised and gratified to hear the heart with greater clearness than he had by direct application of the ear to the chest. From this paper stethoscope he evolved one of wood. From this has come the electric stethoscope, by means of which the heart sounds can be amplified and heard through a large hall.

Digitalis was introduced to modern medicine by Dr. William Withering of Birmingham, England, who used it professionally as a diuretic in the treatment of dropsy, having found it to be the chief ingredient of a family recipe which had long been the secret of an old woman of Shropshire.

The Pharmacist's Part

This account of how a few of our medicines and methods of diagnosis were discovered may serve as an index to further study. But brief as such stories are they contain much of interest and will serve the purpose of bringing home the fact that discoveries are of no practical use unless they are put into application. Jenner's discovery would save no one from smallpox if the vaccine was not available for physicians. Ether must be available for surgeons if patients about to undergo operations are to be relieved of pain. Here is where the corner pharmacist plays his big, silent part in the progress of the healing art and in the field of lifesaving. He manufacturers or promptly stocks new discoveries, thus making them generally available.



AN OLD STETHOSCOPE, a modification of the paper cylinder first used by Laennec in 1819, is shown in this photograph from the U. S. National Museum.

FROM THE PAST TO PHARMACY RESEARCH OF TOMORROW

by GEORGE D. BEAL

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

FOUNDATION PROPOSED AS COOPERATIVE PROJECT TO PROMOTE PHARMACEUTICAL RESEARCH. ASSAYS NEED A STANDARDIZED ASSAYER

PHARMACEUTICAL research in America began over a century ago during the period of botanical exploration. Much of the pioneer work in inorganic chemistry had been done, and chemistry had become a science. At the beginning of the last century, interest was arising in the constitution of plants as well as their classification. Courtois discovered iodine in the ashes of seaweed, Derosne obtained a crystalline material from opium, the basic nature of which was recognized by Serturner, who named it morphine, and Pelletier and Caventou isolated quinine from cinchona. Pharmaceutical manufacturing, save for chemical salts, was almost entirely on a retail basis.

Organic chemistry as such was born about 300 years ago. The early experimentation was upon the products of animal and vegetable origin. Those having medicinal properties were then of greatest interest, and so influenced the beginning of synthetic research. Some of the most distinguished organic chemists of that time were pharmaceutical chemists by profession, as were their predecessors in inorganic chemistry.

During this period of chemical development, some pharmacists began to manufacture on a more generous scale. Extractions, distillations and similar operations were performed in larger bulk quantities, and some hand operations were carried out mechanically. Growing demands for these products encouraged the progress of pharmaceutical engineering. Manufacture on a large scale emphasized the need for scientific control. Control operations were at first only chemical in nature, but with better knowledge of the action of drugs have come bioassays, these studies crystallizing as the science of pharmacodynamics, improperly called pharmacology.

The biological era in pharmaceutical research begins with just about the present century, although systems of vaccination and bacterial therapy stem back farther, even to the time of Jenner. Last of all we have the synthetic period, when chemical constructions and reconstructions of molecular groupings are taking the place of natural drugs with their high contents of inert materials.

The above represent stages in pharmaceutical research progress, and they have developed separately as tools, but in their applications all are intermingled. As one example, the therapeutic properties of a metal are improved by exhibiting it as a component of an organic molecule. By such means, its solubility, mode of absorption, and elimination are altered or regulated, its toxicity reduced, or its specificity increased.

Pharmaceutical chemistry produces agents to affect physiological processes. These life processes are both physical and chemical; therefore, pharmaceutical research employs the methods of many sciences. A person cannot, in any reasonable time, discuss all the divisions of pharmaceutical research. Only a few scattered thoughts can be presented here.

The discovery of compounds in drug plants having properties as specific as those of the plants themselves caused much of the earlier work in organic chemistry to be directed toward the study of drugs. Attempts at the synthetic production of these principles led to chemical discoveries of industrial as well as medicinal value. Chance observation of the physiological properties of new compounds, as of ether, chloroform and chloral, kept organic chemistry closely linked to pharmacy for a long time. Probably the four great outlets for the synthetic skill of the organic

Presented before the American Pharmaceutical Manufacturers Association, Hot Springs, Va., 1943.

chemist today are drugs, solvents, dyestuffs and plastics, with drugs, as the oldest member of the family, maintaining a constant degree of interest.

In synthetic research as applied to pharmacy, there have been at least three aims. The first has been the reproduction of natural derivatives, the second the production of analogous compounds of equivalent or superior activity from which certain faults should be absent, and the third the discovery of new drugs of novel and unusual properties. In the first class, some of the products have been salicylic acid and methyl salicylate, thymol, menthol, camphor, epinephrine, ephedrine, ascorbic acid, thiamine and riboflavin. One of the hardest tasks has been to reproduce the optical activity of natural products. Nature has a way of producing optically active forms that man has found it difficult to imitate.

An important purpose of the first type of syntheses is to improve yields, to simplify purification, or to free from reliance upon foreign sources. In the production of synthetic camphor from American spirit of turpentine, we have freed ourselves from the Japanese monopoly of natural camphor, and were fortunate to have done so long before the war clouds began to gather. The synthetic product is optically inactive, but this is one instance where such inactivity is no drawback to medicinal use. The economic experience with camphor is being repeated today with menthol, and, although they do not fit in this chemical class at all, we may anticipate the same outcome in the replacement of silk by nylon and of natural rubber by synthetic elastomers.

Improving Nature

In the second class of compounds are such useful drugs as procaine, homatropine, benzedrine, compounds having vitamin K activity, and the synthetic sex hormones. It may be questioned whether the synthetic antimalarials atabrine and plasmochin belong here or in the third class, but they do partake of the physiological properties of quinine, and their synthesis was in a measure suggested by the knowledge of the structure of quinine.

Synthetic replacements have been free of some of the faults of their natural predecessors. Synthetic procaine is said to be devoid of two of the serious objections to cocaine, having lower toxicity and being non-habit forming. Homatropine is claimed to be more specifically mydriatic than atropine, and benzedrine has a degree of volatility that makes it a convenient topical vasoconstrictor by inhalation.

Vegetable Veterans

The synthesis of analogues of natural drugs has not led to the effacement of the drugs. Quinine is the standard among antimalarials and is still obtained from cinchona bark. Digitalis seems to be essential in the treatment of cardiac disorders, and ergot is much relied upon by the obstetrician. Cocaine and morphine, though habit forming, are regarded as the standard of performance, respectively, for local anesthetic and hypnotic action. And, excepting for phenolphthalein and the saline laxatives, practically all the useful cathartics are of vegetable origin. It also happens that some of the earliest synthetic replacements have been the most successful in a particular field. For example, in spite of much extensive research and many elaborate claims, it is hard to picture any replacement for cocaine more successful than procaine.

The third class of synthetics, and the one that excites the imagination the most, is that of entirely new means of obtaining desirable therapeutic effects. Ether itself was not an American discovery, but its anesthetic use was, and much of the research on other gaseous anesthetics has been carried on here. Barbital, the first successful malonylurea hypnotic, came from Europe, but most of its successors are from our laboratories, particularly those for intravenous anesthesia.

I have referred earlier to the intermingling of organic with inorganic chemistry. The most notable examples have been the organic arsenicals, but the mercurials and the bismuth compounds have likewise been of great interest. Now comes the long list of derivatives of sulfamic acid with their many anti-infective uses. Certainly, we have only scratched the surface of synthetic possibilities.

An examination of the calls made upon the chemical section of the U. S. P. Revision Committee during the past three years is indicative of the present demands upon pharmaceutical research. Some of the questions raised have been those that come at the end of any revision

period, resulting from lack of attention to publicity given proposed standards. Sometimes proposed standards are too drastic, or inapplicable to certain manufactured products. Obviously it is impossible for a practical working committee to be familiar with all manufacturing conditions, especially if some production practices are trade secrets. An effort has been made to bring proposed changes to wide public attention, but serious thought is often not accorded proposed changes until they appear in page proof or actually attain official status. In general, these problems are rather easily adjusted because the technical representatives of the ethical manufacturers have a sympathetic and coöperative spirit.

War Problems

A second group of problems has arisen from the effect of national war effort and international war upon regular sources of supply. We are fortunate that we had already established the synthetic production of camphor and menthol, and that atabrine and plasmochin had been established as antimalarials. Researches by Philippine and League of Nations health authorities have developed the synergistic effect of the crystalline cinchona alkaloids when used as mixtures for antimalaria effect. Taken originally as a mixture containing approximately 25 per cent of anhydrous quinine under the name of totaquine, it was said to have roughly 67 per cent of the efficacy of quinine alone. The present line of thought calls for 7 to 12 per cent of quinine in from 70 to 80 per cent of total crystallizable cinchona alkaloids, and it is being hinted that quinine is unnecessary in the mixture.

This knowledge is particularly timely when our supply of East Indian bark has been lost and the bulk of the South American bark is of low quinine content. The richness of the East Indian bark has been a tribute to the ability of plant breeders. If the totaquines of low or insignificant quinine content prove to be efficacious as antimalarials, pharmacologists should begin a reëxamination of the optical isomers or racemic forms of other therapeutically active compounds which may be produced synthetically. The success of the new antimalarials has been brought about in part by new knowledge of the life stages of the malarial parasites. Based upon this knowledge, it has been possible to use quicker laboratory methods for the trial evaluation of new compounds, thereby rejecting at once those of no value, and modifying those of some promise in order to enhance their value.

Looking at the synthesis and evaluation of drugs as an outsider, it would appear that knowledge of their value comes more quickly from the study of their effects by physiologists than by toxicologists. This is particularly true of the study of drugs used for specific organic effect. It has always seemed irrational that so many bioassays are based upon the determination of lethal doses. A scientist can appreciate that such assays result from the present condition of knowledge, but laymen frequently question why drugs expected to preserve life are measured by their ability to destroy it.

I have listened, for example, to many learned lectures and conferences on the assay of digitalis and its products. Each method or variation proposed for the bioassay has been proclaimed as the one which resolved all doubts about the potency or stability of the drug. Then comes a report upon collaborative assays carried out in many laboratories by experts, in which reports from reputable workers ascribe 100 per cent variations to a pair of samples that, unknown to them, came from the same lot. The variations in individual animal responses prove to be so wide that only mathematical treatment by experts can compute the probable correct value. Even the question of obtaining an adequate supply of assay animals becomes very serious. Exactly the same situation exists in the biological evaluation of vitamin preparations.

Imperfect Assays

The justification of biological methods of assay is found in the fact that they attempt to measure, under standard conditions, on animals or plants uncomplicated by pathological conditions, the effect that the same product will have when used for therapeutic or protective purposes. When testing protective agents, such as the nutritional vitamins, the assay methods are most nearly justified because pathological conditions are usually absent during treatment. The assumption is still required that the animal response is similar to human response, and the result of individual animal variations must be

taken into account when making the computations.

Fully realizing the incompetence of my judgment because of complete lack of experience, I still feel that a bioassay is not the last word in the evaluation of products used in the treatment of pathological conditions. The experimental animal, even when artificially injured, cannot altogether reproduce the pathological state of the human patient. Some of us have said jestingly that a poor chemical assay, where available, will give more competent results than a good bioassay.

Better Chemistry

Such a jest is obviously unfair. No chemical assay of a drug can be performed without knowledge of the existence therein of an identified chemical individual or group of known reactivity. It also requires the assumption that the therapeutic value of the drug depends quantitatively upon or is in some way proportional to the content of this specific principle or group. The responsibility for the use of a biological assay of a therapeutic agent must therefore be placed upon the shoulders of the chemist. He has either failed to separate and characterize adequately the active agent or group, or, the principle being known, he has been unable to devise characteristic quantitative chemical reactions for its determination. So, if we chemists object to the insufficiency of biological assays, we must bestir ourselves to obtain adequate chemical information, backed by clinical substantiation.

There is one common fault in the practice of both methods of assay. That is the inability of the English language, or of those who write or read it, to convey thought with sufficient precision. In directions for a chemical test, you frequently find the expressions "evaporate to a small volume," "acidify," "warm," "ignite," and many others like them. These may seem very precise, but there is nothing quantitative about them. The best that can be said is that one who is "skilled in the art," as patent law puts it, will presumably in his repetitions perform these in essentially the same manner. But his fellow worker, also skilled in the art, will probably depart a trifle in obtaining what he regards as precision.

I have suggested several times that there is a frequent need for the standardization of the assayer as well as of the method or the reagent. Very frequently, a proposal for a chemical analysis is pronounced unworkable by other analysts, yet if they come together in the laboratory to observe each other's technique, the lack of agreement in procedure is found and corrected. There are many conferences and summer seminars to discuss recent developments in science. It would be useful to devote some conferences to the study of laboratory procedures, where methods of assay would be practiced by a group of experienced workers in turn and in the presence of each other. This, I believe, would clean up many present-day controversies. There is an old Latin proverb that fits here, "*quid custodes ipsos custodiet*," which, somewhat freely translated, is "who shall watch the watchmen?"

There appears to be too much restraint exercised in the relationships between industry and education. In medical and pharmaceutical education, the suspicion still seems to exist that an industrialist, in general, is after no good end. Evidences of this keep cropping out in conversations with good friends who in most of their habits of thought are quite rational. If this sort of suspicion does exist, it is as unfortunate as it is generally unfair, and requires analysis for its elimination. Such ideas usually spring from lack of intimate knowledge of what is on the other side of the hill. Possibly the reason chemists and engineers have less suspicion of industry is because they habitually look to industry for the absorption of those who do not go into educational work, which means the majority of those going through college. Industrial organizations now establish graduate fellowships right and left in the hope of providing more trained research specialists rather than of securing immediate profit from new discoveries. In pharmacy and medicine, on the other hand, graduates more frequently go into professional practice on their own account, so that to them the industrialist is just another person trying to prevail upon them to promote his wares.

I am very frequently asked where one may have a compound evaluated for physiological effect. Some manufacturers are very fortunate in that they have been able to establish hospital relationships where clinical studies can be made. Others have organized pharmacological divisions that can work in conjunction with the research laboratory for the testing of new compounds.

Some make such arrangements as they can with university workers. But there is a great deal of lost motion for scientific laboratory workers who do not have direct access to adequate pharmacological or clinical facilities.

Need Research Foundation

There do not seem to be many clinical investigators in the medical colleges with hospital affiliations who have the ability, time or inclination to carry on coöperative studies of this kind. There are some men so well known in their fields that the demands upon their time are very great, the laboratory worker losing much valuable time while waiting for reports. There are some of such a scholarly nature that they are always waiting to complete a few more confirmatory or convincing tests before rendering a report. These overlook the fact that preliminary reports with a considerable margin of error will serve to direct further work in the research laboratory. And there are some, I fear, who adhere to a code of ethics that causes them to frown upon contacts with investigators whose products may make a financial return for someone.

Can we not set up a coöperative method to provide pharmacologic and, when justified, clinical guidance to the chemical researcher? This can be done by freeing medical college laboratories from silly ethical restraints, or by providing laboratory foundations to make needed facilities available. A college of pharmacy with facilities of space and money, and with an age, educational and research reputation to command respect would be an excellent place in which to inaugurate an institute of pharmacological research. I find that whenever I suggest establishing a research foundation my college friends begin to ask where they can find a million dollars for a cornerstone. The fellowship system that is now Mellon Institute began with a grant of $500 for a year's study of a laundry problem, and the fellow lived and paid his laboratory fees. It took six years to acquire a frame laboratory of its own, and thirty years to gain a permanent home. Its cornerstone was only a man of integrity, vision and magnetic personality.

The director of such an institute must be able to carry water on several shoulders, for his files will hold much confidential information. There can be some workers who will give all of their time to coöperation with one laboratory. Others must serve several, because some very important discovery may come from a small laboratory. This foundation must serve the small industrialist who cannot maintain a private laboratory, and the college without medical affiliation. But, like the foundation which I represent, it will also serve the company maintaining its own laboratories, in order to give the project investigated a more unprejudiced study.

If the institute could extend itself to study surgical supplies as well, it would serve an even greater need. No reflection upon medical colleges is intended when proposing that the foundation operate in conjunction with a college of pharmacy. The opportunity has existed for a good many years, but is apparently not welcomed; therefore, why not establish it where it is more certain that an interest will be found in the constitution and character of new drugs?

I have often wondered if the plan of the exchange professorship could be used to promote better relations between pharmaceutical education and industry as it has between other educators. A junior member of the research or operating staff of a manufacturing establishment could be exchanged for a period of a year for a member of the permanent faculty of a school of pharmacy. The exchanges should be as far as possible on a basis of equal salaries, but with added compensation to each because of unusual expenses created. The persons exchanged should have the same general interests in order to step into the other's position.

Exchange Professors

These exchanges might cost less for the two men exchanged than the granting of two fellowships. It would put each man into a new environment where he would be on terms of equality with those having the same general interests but a different form of specialization. It would give each man some appreciation of the problems which the other group must solve. It would familiarize the teacher with practical problems in the procurement and handling of materials, and with the differences that exist between small-scale preparation as carried on in the college laboratory and the manufacture of the same commodities in bulk where day after day the same uniformity of product is required.

In general, the result should be to produce a sympathetic understanding of all manufacturing problems, and aid him to view understandingly all that goes on to put finished pharmaceuticals on drugstore shelves.

The industrialist could, from his fuller practical experience, present both to students and faculty a practical view of professional problems. He could suggest new methods of approach to classroom and laboratory problems. He would benefit from a scholarly discussion of fundamental investigation. He would be able to enrich his classroom discussion with a host of practical examples of application.

The progress of pharmacy depends upon education and research. Retail pharmacy is publicly condemned for the commercialization that exists therein. It may be high minded to criticize the retailer for his weaknesses, but should we not recognize the fact that there are those above who have encouraged and catered to those weaknesses? Someone has had to provide the deals, the counter displays and the lay advertising, and encourage the cut prices and the competition that creates or encourages what is considered the objectionable part of commercial pharmacy. Research in the manufacturers' hands must always have some element of practicality about it. Along with practical industrial research, there must be painstaking, scholarly, fundamental research of the type that can be so well done within college environs. Pharmaceutical manufacturing exists because of the profession of pharmacy, and its returns are gathered for it by the profession. It is most essential therefore that the industry which profits most from the practice of pharmacy as a profession should continue to fertilize that field by plowing back into the educational program of pharmacy a just proportion of its earnings.

PHARMACY HONORS SCHEELE

The dramatic discoveries of one of the greatest pharmacists of all time shine all the more brightly against the humble background of his life as told in pictures and prose by Dr. George Urdang in THE APOTHECARY CHEMIST: Carl Wilhelm Scheele (*American Institute of the History of Pharmacy*, Madison, Wis., $1.25). This slim volume lays no claim to being an exhaustive and exhausting biblical tome on the great man. But with a wholehearted admiration that approaches reverence, the author has compiled a concise Scheele-catechism. Publication is under the joint auspices of the American Institute of the History of Pharmacy and the AMERICAN PHARMACEUTICAL ASSOCIATION.

Two centuries ago marks the beginning of the story, when Scheele was born at Stralsund, then a Swedish city. At 14, young Carl decided to become a pharmacist, a decision that is not only a landmark in the history of pharmacy, but of the world. It was only shortly after, that Scheele began the studies and experiments that were to lead to the discovery of chlorine, manganese, oxygen, and a long list of organic and inorganic compounds. He isolated glycerin and milk sugar for the first time. He invented new processes for preparing such substances as phosphorus, calomel and magnesia alba. These and other achievements paved the way for fellow pioneer chemists rapidly to extend the frontiers of chemical knowledge.

Throughout his life of triumphs, Scheele never forsook pharmacy. He worked in a number of apothecary shops, conducting his research in conjunction with full-time prescription work. Dr. Urdang succinctly traces this brilliant career which ended when Scheele was only 43 years old.

A timetable of Scheele's experiments, translated from a German work by the author, is supplemented by a tabulation of his most important discoveries.

Most of the booklet (36 pages) is devoted to historical illustrations with explanatory captions. The text is readable, the format attractive, but the printing leaves a good bit to be desired.

NEW DISPENSATORY PUBLISHED

A reference work that has been on the pharmacist's bookshelf for 110 years is now off the press in the twenty-third edition: THE UNITED STATES DISPENSATORY (*J. B. Lippincott Co.*, Philadelphia, $15). The Dispensatory continues to grow in stature, now a well-organized 1900-page volume including much of the U. S. P., N. F., N. N. R. and British Pharmacopœia.

Dr. H. C. Wood of the University of Pennsylvania and Philadelphia College of Pharmacy and Science is again chief editor, this time collaborating with Dr. Arthur Osol of the Philadelphia College of Pharmacy and Science. The editors were assisted by Dr. Louis Gershenfeld, also of the Philadelphia College of Pharmacy and Science, and Dr. Heber W. Youngken of the Massachusetts College of Pharmacy.

Rapid advances in pharmacy and medicine since the last edition was published seven years ago have necessitated much revision. U. S. P. XI and N. F. VII material includes changes through the first supplements. Abstracts of N. F. galenicals have been supplanted by the formulas in full in the twenty-third edition.

British Pharmacopœial drugs have been brought up to date as far as the first five addenda which were published before the Dispensatory went to press. Unofficial drugs recognized in the N. N. R. are listed as of the 1942 edition. Special mention has been made of those changes, omissions and replacements which have been brought about by war conditions.

New general articles on groups of chemically related active principles include discussions of glycosides, alkaloids, sterids, amino acids and surface-active agents. The use of graphic formulas for organic compounds has been greatly extended throughout the book.

The general plan of former editions has been retained, the book being divided into three sections: (1) official drugs; (2) unofficial drugs; (3) processes, reagents, solutions and tables.

PHARMACY MANPOWER

A study of pharmacy manpower in one state that should be seen by pharmacy officials in every state of the nation, and that may well serve as a model for similar projects elsewhere, is PHARMACY MANPOWER IN OHIO (*Ohio State University Bureau of Business Research*, Columbus, O., *$2*).

The survey was initiated by the Ohio State Board of Pharmacy with the assistance of the State Association and the wholesale drug trade. Questionnaires were sent to every registered pharmacist. Back came replies from 96.7%. The information thus garnered should be invaluable to Selective Service officials who have been hampered in maintaining essential pharmaceutical service in many areas by a lack of pertinent, concrete facts. Further than that, the report will be of value in a host of ways to Ohio pharmacy. For example, it breaks down the distribution of pharmacists county by county and city by city, showing the pharmacist where his services are most needed by the population. It reveals where competition for prospective store owners will be least keen, and where there will be adequate demand to support professional services.

The data are analyzed according to type of employment, draft and dependency status, location, age and other characteristics. Such statistical breakdowns would make a complicated task for most pharmaceutical organizations —perhaps inadvisable if the results are to be fully accepted by government agencies. In the case of the Ohio study, the Bureau of Business Research at the local state university took over the mass of data for transformation into a concisely written 88-page report with 22 charts and tables. Such a coöperative project might be developed elsewhere, or, as an alternative, a commercial firm skilled in statistical analysis could be called in for the orderly marshalling of facts which makes the difference between an illuminating report and a hodge-podge of figures.

Of the 5701 pharmacists polled, we see at a glance that 613 work outside of Ohio. Of the remaining 4768 pharmacists, 262 are women. Of the total number employed, 88.2% are in retail pharmacies, 2.8% in hospitals, 4.7% in sales work, etc.

Only 51% of Ohio pharmacists in the armed forces are "rendering pharmaceutical service," the study indicates. This figure is based on 277 replies from the 320 Ohians who were in the armed forces at the time of the survey. This seems to confirm the opinion of many that the

pharmacist's technical knowledge is not being used in the Service to best advantage. Unfortunately there is no way of knowing to what extent the pharmacist's knowledge is being utilized even though he is not directly giving pharmaceutical service.

COMPOUNDING TEXT REVISED

Completely revised and packed full of aids for the pharmacist as well as the undergraduate tyro, Scoville's THE ART OF COMPOUNDING (*Blakiston Co.*, Philadelphia, $4.75) is now available in the seventh edition. The new version has been prepared by Dr. Justin L. Powers, editor of the Scientific Edition of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION and chairman of the National Formulary Committee, and Dr. George E. Crossen, dean and professor of pharmacy at Drake University.

Chapters have been rearranged to give a more logical sequence and many have been rewritten. Material on adjusted solutions has been expanded to include the simpler methods of calculating isotonicity and freezing points. The chapters on vitamins and biological products have been condensed to include only information that is practical for the dispensing pharmacist.

SIMPLIFIED METHODS OF *Wartime Stock Control*

BUYING-BUDGET, RATIONED SHELF SPACE, PROPER INVENTORY HELP SOLVE STORE-OWNER'S PROBLEMS

by PAUL C. OLSEN

EFFECTIVE control of merchandise stocks has always been an exceedingly important but difficult problem in retail pharmacies. In a store with a merchandise stock with a total value of $4000 at cost prices, there are likely to be as many as 8000 different items, counting styles, sizes and colors. Thus the amount of money tied up in many hundreds of these items is very small indeed. Stock control problems have been multiplied by the war. Shortages and the complete disappearance of some merchandise, slow deliveries, changes in the sizes, packaging methods and in the formulas of the goods themselves have all been contributing factors.

In addition to the very obvious complications which are apparent in a retail pharmacy with only a small amount of money tied up in any one particular item, there are the problems created by the characteristic long hours and small scale of the operations of most retail pharmacies. It is manifestly impossible for a pharmacy in which there are only one or two employees including the proprietor to take on the complexities of installing and operating the conventional perpetual inventory system. There just isn't the time or the inclination to maintain such records. It is also a fact that the results in a retail pharmacy could not possibly compensate for the effort required.

Perfectionists may regard as makeshifts the stock control methods which are suitable for use in a pharmacy, but these methods do have the virtue of practicality. For the store owner they offer the satisfaction of simplified operations and extra profits. There never was a time that is more important than right now for such methods. The present sellers' market is bound to end some day. Then people will look more carefully at

Presented by title to the Section on Pharmaceutical Economics, A. PH. A., Columbus meeting, 1943.

the quality of the things that they can buy and the prices they are asked to pay for them. The pharmacy owner who has a lot of his money tied up in goods made to wartime specifications is going to be faced with serious and probably overwhelming problems in getting his money out of these goods when better merchandise becomes available.

Buying Budget

Now as to the stock control methods that are practical to use in even the smallest pharmacies, first, in my opinion, is a buying budget. When I tell retailers in other fields that there are not just a score or a few hundred but thousands of retail pharmacists who are trying to operate their stores without the guidance of a buying budget, they are amazed. The idea of the buying budget is not one which originated in the pharmaceutical field. It is something that has been used with much success and for so long in various other branches of retailing that there it has become routine.

The only things that a pharmacy owner needs to take into account in putting into operation a buying budget in his store are estimated sales and the gross margins that he expects to realize. These estimates of sales and gross margins do not need to be made for more than a month in advance. Therefore errors in forecasts can be corrected quickly. For example, the busy and tired proprietor of a one-man pharmacy estimates that his sales in October will be $1500, and that on these sales he should be able to realize a gross margin of $500. Therefore to replace merchandise which he expects to sell in October he should buy goods that cost him a total of $1000. If he buys more than $1000, he is piling up stock on his shelves that may prove impossible to sell. If he buys less than $1000, he is living off his inventory.

When November 1 comes, the actual results are compared with the October estimates. If more stock was bought than was needed to replace the goods sold in October, that is a plain warning to the proprietor to cut down on his buying in November and a definite indication of just how much to cut down on November buying. If more stock was sold than was replaced, that is an indication that in November the proprietor can be a little more liberal in his buying.

This is the simplest form of buying budget. Any person competent to be the proprietor of a retail pharmacy will recognize quickly that there are decided variations in the gross margins realized from the sale of different kinds of merchandise. These differences are apt to be submerged and overlooked in store-wide estimates. Therefore in any store in which the volume of sales is more than $2000 a month, it is wise to prepare separate buying budgets for the principal departments of the store. It is usually sufficient to make some such division as tobacco, fountain, and a "drug" department representing the rest of the store.

One of the most frequent questions asked in connection with the introduction of a buying budget is, "What about seasonable goods?" That's easy. How long will it take to sell out this seasonal purchase? Suppose it is bathing caps. (This really is a theoretical example but there will come a day when bathing caps are once more available in any quantity that a retailer can pay for.) Suppose the order is given in February for $150 worth. They are to be sold, it is hoped, in May, June and July, with maybe a few left for late summer selling in August. Therefore the buying budgets for May, June and July are each charged with $45 of the $150 purchase and $15 marked off against the buying budget for August.

Provides Fresh Drugs

The prescription department is another place in which simple stock control methods will save many losses from spoiled, deteriorated and obsolete stock. Items bought in bulk containers are marked in code with the date of the purchase. Then it is a simple matter to decide on the quantity the next time the goods are ordered. Without this information it is just a guess because no one, particularly in a small store, can remember or even know the right quantity of prescription items to buy unless he has some kind of records.

For packaged goods this information is most readily made available in a retail pharmacy with a minimum of work by assigning each item definite shelf or storage space. This can be done by simple shelf markers or by designations right on the shelves themselves. The shelf space set aside

thus indicates the maximum quantity of the item that has been found profitable to keep on hand and the quantity to order. This is important because quantity discount propositions of various kinds are going to be revived with a vengeance right after the war has been won.

False Savings

Then it will be a strong-willed pharmacist indeed who can resist the blandishments of the representative who tells him, "But, doctor, don't you see, if you buy three dozen, you get an extra five per cent." The store proprietor who has apportioned shelf space for the various staple packaged articles in his stock doesn't have to rely on memory or hunches in deciding whether or not the three-dozen purchase is a good buy. If he sees that the space allotted to this particular item holds a maximum of two packages, he does not need to investigate any further to realize that his decision to have a maximum stock of two packages of that item resulted from experience that two packages are all he can expect to sell in one or even two months.

A three-dozen purchase therefore means taking on anywhere from eighteen months to a year and a half's stock, all for the sake of a five per cent discount. On the other hand, a five per cent discount can be a very welcome addition to the gross margin and the net profits if the shelf space allotment indicates that the maximum stock to be kept on hand is more than three dozen.

While I speak here of shelf space, the principle is just as readily adaptable to items which are kept in other kinds of fixtures. Small goods that are customarily kept in drawers can have space set aside for them in an amount equal to the maximum stock that is wise to keep on hand.

There are some items, bulky goods and extremely fast sellers, for which it is not practical to keep the entire stock on a shelf in the front end of the store. This fact can be indicated by a symbol on the shelf to remind that reserve stock is to be found in the basement or some storeroom elsewhere. This reserve stock can be arranged in the same manner, with an allotment of space equal to the maximum quantity of the item which it is desired to keep in the reserve stock.

There are some fancy goods for which it is not practical to use the shelf space allotment principle. The very fact that these are fancy goods emphasizes the importance of effective stock control for them. The best way, in the experience of proprietors who have struggled most successfully with this problem, is to depend on want-books. Often with these fancy goods there are only one or two of a kind in the store. In the rush or enthusiasm of selling these big check items an employee or even the proprietor himself is apt to overlook ordering a replacement. The surest reminder is a want-book, conveniently at hand where sales of these items are made. In most stores this means several want-books in different parts of the store so that unnecessary steps won't have to be taken to make notations.

No discussion of effective stock control methods in a retail pharmacy would be complete without mention of the prime necessity of an inventory every year of the entire merchandise stock. Whether the store owner takes the inventory himself or hires outside experts to do the work for him, the results are certain to be worth many times the cost. It is no unusual thing for such an inventory to dredge up hundreds of dollars worth of goods that had been forgotten in the rush of everyday operations.

Let me emphasize that now, as never before, effective stock control is vital to the continued and successful operation of a retail pharmacy. Therefore the wise and alert pharmacist is conducting his store now in a manner which will leave him with a minimum accumulation of wartime substitutes when better goods can be obtained. To be ready for the change he knows there must be adequate stock control methods in his store.

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REMOVING NICOTINE STAINS

Question: I have had several requests for a preparation for removing nicotine stains from the fingers. Can you suggest a formula?

Answer: Two formulas for removing so-called "nicotine stains" are listed by H. Bennett.

(1)	Sodium sulfite	25
	Water	100
	Hydrochloric acid	2
(2)	10% Hydrogen peroxide	10
	Ammonium chloride	1
	Alcohol	5

ADD TRAGACANTH AS DESIRED

Question: I have been having trouble in making the following mixture as thick as the prescriber desires it: Tragacanth ℥ ¾, Ppt. Sulfur gr. 38, Calamine ℥ ss, Zinc Oxide ℥ ss, Camphoræ Chloral ♏ 5, Camphoræ Phenol ♏ 5, Phenol ♏ 2½, Glycerin ♏ 2½, Ol. Rosæ ♏ 5, Ol. Lavender ♏ 5, Ol. Olivæ ℥ 2, Aqua q. s. ad ℥ 8. What are your suggestions as to the best procedure?—L. W., Ohio.

Answer: Although neither the present thickness nor the desired thickness of the preparation is indicated, it is perfectly permissible to increase the amount of tragacanth to provide the viscosity desired. Mixtures of various viscosities could well be obtained in different stores dependent upon the nature of the tragacanth which was used. Official standards do not provide any control for the viscosity quality of tragacanth.

As to procedure, the tragacanth should be mixed with the olive oil and an ounce and a half of water gradually added to provide an emulsion. The other ingredients should be triturated together separately and made into a smooth paste with water. This paste should finally be gradually added to the emulsified oil.

COAL TAR EXTRACT

Question: Please suggest a colorless extract of coal tar that could be incorporated into a suitable ointment base.—L. M., Ohio.

Answer: We suggest the stainless synthetic tar developed by Drs. W. H. Guy, F. M. Jacob and Frank Weber of the University of Pittsburgh School of Medicine. This formula is reported (*Arch. Derm. and Syph.*, July, 1939) to contain quantities of active ingredients equivalent to those in crude coal tar. Petrolatum has been substituted for pitch, and the inert substances and irritating oils have been omitted.

Anthracene	1.10
Naphthalene	10.90
Phenanthrene	4.00
Carbazole	2.30
Picolene, Pyridine, Quinolene, *aa*	0.58
Phenol	0.70
Cresol	0.75
Petrolatum	100.00

The synthetic tar may be used in the same amounts as crude coal tar.

BETTER OINTMENT BASE

Question: We have been having trouble making the following formula into a permanent cream-like preparation without it shedding water. What do you suggest?

Saturated Sol. Zinc Sulfate.....16 oz.
Sol. Vleminckx.....16 oz.
Glycerin..... 1 oz.
Greaseless water-soluble base, q. s.

The physician desires the ointment to have a rose fragrance, but when Rose Water is used the interaction with the sulfides soon destroys the fragrance.—M. M., New York.

Answer: Using the following formula to make the base, we have prepared the ointment on a small scale and it appears to be stable.

Cetyl alcohol.....15.0
White wax..... 1.0
Propylene glycol.....10.0
Sodium lauryl sulfate..... 2.0
Water.....72.0

Melt the cetyl alcohol and white wax in the propylene glycol on a water bath and heat to about 65° C. Dissolve the sodium lauryl sulfate in the water and heat on the water bath to about 65° C. Slowly add the oil phase to the well-stirred water phase and continue stirring on the water bath for about ten minutes. Remove from bath and continue stirring to the point of congealing.

If the ointment is too liquid when the other ingredients are incorporated, a little experimental work eliminating part of the water from the base should produce the proper consistency.

The addition of ionone, which has the odor of violets, appears to mask the odor of the sulfides successfully.

LESS EXTRACTION BLEEDING

Question: What could we supply a dentist to check excessive hemorrhage in dental extractions which is believed to be caused by prothrombin deficiency?

Answer: When due to prothrombin deficiency, vitamin K in doses of two tablets *t. i. d.* three days before, during, and three days after the extractions should be of benefit. It is given with small doses of bile salts to aid absorption.

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CREAM MATERIALS VANISHING

Question: Please send a formula for a good vanishing cream base. As you know, we experience much difficulty in securing the essential materials to compound it.—S. E., Pennsylvania.

Answer: We presume that you wish to use this base as a vehicle for ointments. The best all-around base we have found was described by Mr. Beeler on page 231 of the July, 1942, issue of THIS JOURNAL. Since the cetyl alcohol in this formula may not be available, however, here is a formula from the Pharmaceutical Recipe Book III for a vanishing cream made of simple ingredients which you probably have in stock. Unfortunately it will not stand up as well in the presence of medication as the Beeler base.

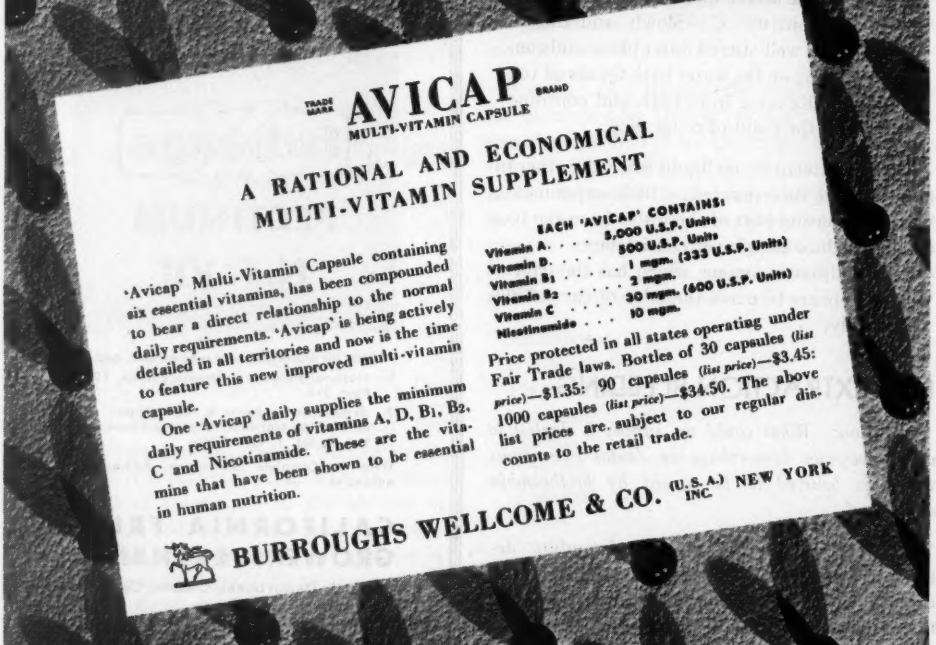
Stearic acid	190 Gm.
Glycerin	75 cc.
Potassium hydroxide	10 Gm.
Perfume, as desired	
Distilled water, *q. s.*	1000 Gm.

Melt stearic acid on water bath at 80° C. Dissolve KOH and glycerin in the water, warm to 85° C., and pour gradually into the melted acid, stirring briskly. Keep at constant temperature and continue stirring for 10 minutes to assure complete saponification and absence of free alkali. Then remove the heat and stir until cold, at the same time incorporating the perfume. Beat for a time, preferably by mechanical means, and then place in jars or tubes.

PAN-CAKE COMPOSITION

Question: Please advise us as to what pan-cake make-up contains.—S. G., California.

Answer: The composition of the various types of pan-cake make-up on the market is covered by several patents. The base consists largely of pigments (such as titanium), zinc oxide, talc and kaolin, plus organic and inorganic color lakes. The binder consists of polyalcohol fatty acid derivatives (such as glycerol or propylene glycol stearate), which are self-emulsifiers.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Druggists' Digest

OF NEW FORMULAS, RECENT PHARMACEUTICAL DEVELOPMENTS, AND OTHER PROFESSIONAL DATA

CHEMICAL CURE FOR TB MAY BE STEP NEARER

The chemical cure for tuberculosis, long promised for the prescription shelf, may be a step nearer, it appears, from an Abbott Laboratories report (*Science*, Oct. 15) by Dr. George W. Raiziss. Diasone, or disodium formaldehyde sulfoxylate diaminodiphenylsulfone, "produced the most beneficial" results compared to other promising compounds, including promin, when administered to tuberculous guinea pigs.

Diaminodiphenylsulfone is toxic to mice, but can be detoxified, Dr. Raiziss discovered, by combining it with sodium formaldehyde sulfoxylate. The detoxification does not reduce its bactericidal power. The diasone thus produced is as effective as sulfanilamide in mice for curing streptococcus infections, and almost as effective as sulfadiazine in curing type II pneumonia. Its most important action, however, is its effect on experimental tuberculosis in guinea pigs.

ACTINOMYCIN MAY FIND USE AS RAT POISON

Actinomycin has been given up as a bad job as a bactericidal agent in the treatment of human disease, but may emerge in a new role as rat poison. The lethal substance, produced by a bacterium of the genus *Actinomyces*, was discovered in the course of researches by Dr. Selman A. Waksman and his associates at Rutgers University and at the Merck Institute of Therapeutic Research. When Dr. Waksman and his co-workers tried actinomycin on various bacterial cultures they found it highly bactericidal. *In vivo* it was another story—less effective and killed the test animals within 15 or 20 hr.

The M. L. D. for rodents is one part by weight to a million parts of the animal's body weight. This potency led to its consideration as a rat poison. The present problem is quantity production at low cost. As a possible step toward synthetic production, actinomycin has been isolated as crystals and a partial analysis made. The substance separates into two parts designated as actinomycin A and B. A provisional formula established for the A portion is $C_{41}H_{66}N_8O_{11}$.

INDISCRIMINATE TOPICAL USE OF SULFAS DANGEROUS

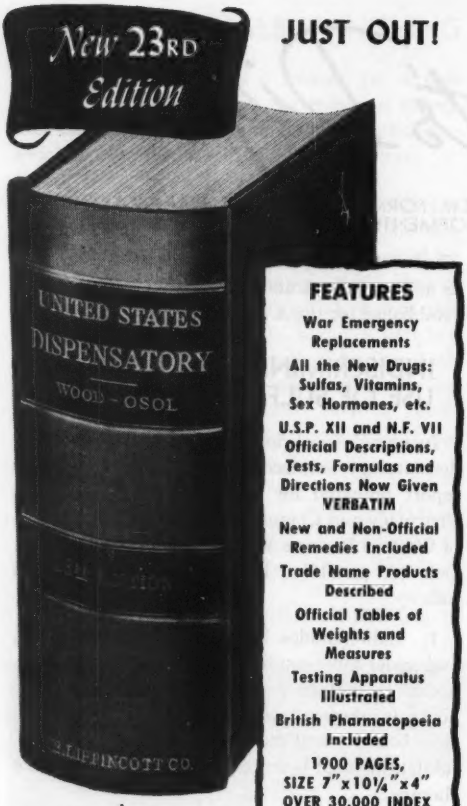
Increased local use of the sulfonamides in dermatology emphasizes the importance of the report prepared for the A. M. A. Council on Pharmacy and Chemistry by Dr. Harold N. Cole of Western Reserve Medical School (*J. A. M. A.*, Oct. 16, p. 410). It may be summarized as follows:

1. Sulfonamides have a local bacteriostatic, and under some conditions probably bactericidal, action in certain infections of the skin. This action is interfered with by excess pus cells, secretion, bacteria and crust formation. Hence careful debridement is an essential to all sulfonamide therapy.

2. Sulfonamides act particularly well locally in powder form in chancroidal infection and in an oil-in-water emulsion base in impetigo, in ecthyma and in acute pyococcic infections. However, they should not be used in these conditions, except in chancroidal infection, until other measures have failed. Most investigators prefer oil-in-water emulsions in which the sulfonamide is suspended or dissolved in an aqueous phase because it allows an even distribution of contact between the drug and the site being treated. This results in a lower surface tension; the compound mixes readily with the exudate and is easily removed on washing.

3. In the light of present data sulfonamides should not be administered locally for more than five days because of the danger of sensitizing the individual and perhaps later precluding internal sulfonamide therapy where the situation may involve a far graver disease, for example, a pneumonia or a bacteremia.

4. The use of sulfonamide ointments should be limited to use directly under the care of a physician.



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PENICILLIN SUCCESSFULLY USED AGAINST SYPHILIS

First news that penicillin, the bactericidal chemical from a common mold, *Penicillium notatum*, may prove the weapon that will eventually conquer both syphilis and gonorrhea, was announced at the meeting of the American Public Health Association in New York.

Apparent cures of four cases of early syphilis by penicillin were reported by Dr. John F. Mahoney, Dr. R. C. Arnold and A. Harris of the U. S. Public Health Service's Marine Hospital on Staten Island. Other patients are now being treated, but in only four cases has enough time elapsed for the doctors to be sure the disease has been cured. The penicillin is injected intramuscularly every four hours, day and night, for nine days. At the end of the first seven hours of this treatment, spirochetes can no longer be found in the syphilitic sores. Blood tests are strongly positive at the start, negative by the 15th day. By the 100th day after treatment had been stopped, no trace of the disease could be detected in the patient's blood by any of the ten most delicate tests for this disease now known.

This speedy cure of syphilis can also be achieved, but not so safely, by the intensive treatment methods devised in recent years. These methods all depend on giving the patient massive doses of arsenic in some form and are consequently dangerous. Penicillin seems to be absolutely safe.

No one using it has yet discovered any sign of a poisonous effect from this mold chemical. Some untoward reactions which showed up during clinical trials were discovered to be due to a substance introduced during a filtration process. This difficulty has been eliminated from present production techniques.

Some patients getting it for syphilis felt a little sick and feverish the first day but that, Dr. Mahoney explained, was due to the large-scale destruction of syphilis spirochetes and not to the penicillin itself.

Gonorrhea is also yielding to attack by penicillin but that is not so surprising. The germs that cause gonorrhea belong very far down in the scale of living organisms. The spirochetes of syphilis are much higher in the biologic scale, close to the protozoa. For a chemical to be able to kill such higher forms of life without carrying any threat to human life is remarkable. Only the fact that the medical scientists have had long experience in the anti-syphilis fight and have facilities and ability for doing precise work makes them feel that successful results of treatment in only four cases can be presented as cures.